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I. INTRODUCTION

Lilly's motion for judgment as a matter of law or new trial, Dkt. 375 ("Lilly Br."), ignores the heavy burden that Lilly bears in seeking to overturn the jury's findings. Rather than identifying critical legal issues for the Court to consider, Lilly attempts to relitigate the entire case (with the exception of infringement, an issue that Lilly should have conceded long ago), inviting the Court to re-weigh the evidence and, in many cases, ignoring the evidence that the jury heard supporting UroPep's case. This is not the proper function of post-trial motions.

Lilly's post-trial brief also persists in making many of the same mistakes that plagued Lilly's pre-trial motions and trial presentation. For example, Lilly persists in its misunderstanding of the nature of the invention of the '124 patent, wrongly treating the '124 patent as an invention of novel compounds. Lilly's written description and enablement arguments are fundamentally based on the misguided notion that, in order to satisfy the requirements of § 112, UroPep needed to describe, and enable the synthesis of, every conceivable PDE5 inhibitor. *See, e.g.*, Lilly Br. at 15-25; 27-37. But this Court long ago rejected Lilly's misunderstanding of the invention. *See* Dkt. 149, Mem. Op. & Order at 30 (the '124 patent claims "are directed to the use of PDE V inhibitors to treat BPH, not to the discovery of PDE V inhibitors themselves.").

Similarly, Lilly misunderstands the advanced state of the art at the time of the invention of the '124 patent. Lilly's arguments on written description, enablement, and indefiniteness all ignore that a person of skill in the art would have been aware of hundreds of selective PDE5 inhibitors, would have been familiar with IC₅₀ selectivity assays like those described in the patent, and would have known how to conduct routine dose-ranging studies to determine the amount of a PDE5 inhibitor to administer for the treatment of BPH. On the other hand, Lilly's obviousness arguments ignore the significance of the UroPep inventors' discovery of the

presence and functional role of PDE5 in the prostate, and their application of that discovery to the creation of a novel treatment for BPH.

Lilly also rehashes legal arguments that this Court has already rejected. Lilly's written description, anticipation, indefiniteness, claim construction, and evidentiary arguments all raise issues that the Court has already found in UroPep's favor. Lilly fails to identify evidence from trial that would warrant revisiting any of those rulings.

II. LEGAL STANDARDS FOR JMOL AND A NEW TRIAL

Whether to grant or deny a motion for judgment as a matter of law is a procedural issue falling under the law of the regional court. *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1346-47 (Fed. Cir. 2012). In the Fifth Circuit, "JMOL may only be granted when, 'viewing the evidence in the light most favorable to the verdict, the evidence points so strongly and overwhelmingly in favor of one party that the court believes that reasonable jurors could not arrive at any contrary conclusion.'" *Core Wireless S.A.R.L. v. Apple Inc.*, No. 6:12-CV-100-JRG, 2015 WL 6694034, at *1 (E.D. Tex. Nov. 3, 2015) (quoting *Versata Software, Inc. v. SAP Am., Inc.*, 717 F.3d 1255, 1261 (Fed. Cir. 2013)). "In evaluating a motion for judgment as a matter of law, a court must 'draw all reasonable inferences in the light most favorable to the verdict and cannot substitute other inferences that [the court] might regard as more reasonable.'" *Id.* at *2 (quoting *E.E.O.C. v. Boh Bros. Const. Co., L.L.C.*, 731 F.3d 444, 451 (5th Cir. 2013)). "[C]redibility determinations, the weighing of the evidence, and the drawing of legitimate inferences from the facts are jury functions, not those of a judge.'" *Id.* (quoting *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150 (2000)).

"A new trial may be granted in cases in which the district court 'finds the verdict is against the weight of the evidence, . . . the trial was unfair, or prejudicial error was committed in its course.'" *Bianco v. Globus Med., Inc.*, No. 2:12-CV-00147-WCB, 2014 WL 5462388, at *6

(E.D. Tex. Oct. 27, 2014) (quoting *Smith v. Transworld Drilling Co.*, 773 F.2d 610, 612-13 (5th Cir. 1985)). “However, ‘[a] motion for a new trial should not be granted unless the verdict is against the great weight of the evidence, not merely against the preponderance of the evidence.’” *Id.* (quoting *Dahlen v. Gulf Crews, Inc.*, 281 F.3d 487, 297 (5th Cir. 2002)). When deciding a motion for a new trial, “[t]he Court must view the evidence ‘in a light most favorable to the jury’s verdict, and [] the verdict must be affirmed unless the evidence points so strongly and overwhelmingly in favor of one party that the court believes that reasonable persons could not arrive at a contrary conclusion.’” *SSL Servs., LLC v. Citrix Sys., Inc.*, 940 F. Supp. 2d 480, 486 (E.D. Tex. 2013) (quoting *Dawson v. Wal-Mart Stores, Inc.*, 978 F.2d 205, 208 (5th Cir.1992)).

III. WITNESS CREDIBILITY

Lilly’s JMOL motion is primarily directed to issues of invalidity, on which Lilly had the burden to come forward with clear and convincing evidence. Lilly’s key invalidity experts – Drs. Roehrborn and Rotella – were repeatedly impeached at trial. “A reasonable jury could have determined that [Lilly’s experts were] impeached during [their] testimony and, therefore, lacked credibility.” *Inline Connection Corp. v. EarthLink, Inc.*, 684 F. Supp. 2d 496, 537 (D. Del. 2010 (denying JMOL motion for infringement in part because jury could have disregarded plaintiff’s expert’s testimony). *See also Rembrandt Wireless Tech., LP v. Samsung Elecs. Co.*, 853 F.3d 1370, 1378-79 (Fed. Cir. 2017) (“The jury was, of course, free to credit [one expert’s] testimony and reject [the other’s].”). Absent credible evidence of invalidity, Lilly failed to carry its burden of proof, let alone show that no reasonable juror could have found for UroPep.

As discussed below, the jury’s verdict was also supported by substantial evidence. In the Fifth Circuit, when there is “conflicting expert testimony,” the court “must infer that the jury found [the prevailing party’s] experts to be credible and persuasive,” and defer to the jury’s credibility determination. *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1362

(Fed. Cir. 2012) (citing Fifth Circuit law). But, especially on invalidity issues where Lilly had to present clear and convincing evidence, the jury was free to reject Lilly's arguments based solely on a determination that its experts supporting those arguments were not credible.

For example, Dr. Roehrborn's cross-examination exposed several contradictions the jury could have relied on to conclude that he lacked credibility. Despite saying that Horny Goat Weed – as described in the Cheung reference – is an effective treatment for BPH, Dr. Roehrborn admitted that in thirty years as a practicing urologist he has never recommended Horny Goat Weed to a patient. Ex. A, Trial Transcript ("Tr.") at 562:25-563:10. Nor had he ever referenced the Cheung article or its teachings to a single patient. *Id.* at 563:11-15. Dr. Roehrborn was also forced to admit that the 2010 American Urological Association Guidelines for the Management of BPH (a guideline panel he co-chaired) stated that "alternative medicines" like Horny Goat Weed are not recommended for the treatment of BPH. *Id.* at 565:9-567:9.

Dr. Roehrborn was impeached in other areas, too. For instance, he said that for someone of ordinary skill working in the field in 1997, "it would have been obvious to expect the presence of PDE5 in the prostate." *Id.* at 482:6-14. But on cross, he admitted that in 1997 he was not an expert in PDEs and had not conducted any research on them. *Id.* at 608:9-14. Further undermining the credibility of Dr. Roehrborn's obviousness opinion is the fact that none of the articles supporting his opinion stated that PDE5 was present in the prostate. *Id.* at 600:4-12. The jury could have reasonably discarded Dr. Roehrborn's testimony as lacking credibility.

Dr. Rotella's cross-examination was more of the same. He admitted that by July 1997 he had less than two months' experience with PDE5 inhibitors. *Id.* at 777:9-778:2. Before then, Dr. Rotella had no relevant experience – a fact he resisted until being impeached with a prior deposition transcript in which he admitted this lack of experience. *Id.* at 780:4-781:2.

In addition, when confronted with a document his expert search agency used to promote his services, he claimed to have never seen it before. *Id.* at 827:23-828:24. Upon learning that the document was Exhibit A to his expert report, Dr. Rotella claimed that he had “paid little or no attention” to it. *Id.* at 828:25-829:10. This “Expert at a Glance” document promoted one of Dr. Rotella’s patents from 1998. *Id.* at 828:4-19. That patent includes a lengthy list of treatments for which a PDE5 inhibitor would be useful, but omits any reference to the treatment of BPH. *Id.* at 800:3-801:12. Dr. Rotella struggled to reconcile that omission with his prior testimony that pre-1997 art rendered the ’124 patent obvious. *Compare id.* at 797:9-15 *with id.* at 801:13-802:1. He also struggled to defend his obviousness opinion when confronted with his 2002 article about potential applications of PDE5 inhibitors, which also neglected to mention BPH. *Id.* at 807:11-14. Most striking of all was how far Dr. Rotella was willing to go to defend his in-court opinion that the ’124 patent is invalid because it has insufficient quantitative data. Dr. Rotella agreed that his 1998 patent also has “zero quantitative data.” *Id.* at 840:6-21. But rather than admit that this fact undermined his opinions regarding the ’124 patent, he chose instead to assert that his own patent might be invalid. *Id.* at 840:6-841:3.

Lilly itself appears to have recognized the significance of the attacks on Dr. Rotella’s credibility, choosing not to mention Dr. Rotella’s name in its closing arguments. *See id.* at 1456:21-1483:6. Thus, the jury’s verdict concerning the validity of the ’124 patent may have been based on Lilly’s failure to satisfy its burden of proof.

IV. WRITTEN DESCRIPTION

Lilly argues that claim 1 of the ’124 patent fails the written description requirement for three reasons. First, Lilly attacks the “narrowness” of claim 1, arguing that the specification describes treating multiple prostatic diseases with inhibitors of PDEs 1, 4, and 5, but does not support the “narrowed” invention of a PDE5 inhibitor used to treat BPH. Lilly Br. at 12-15.

Second, Lilly attacks the breadth of claim 1, arguing that it covers all PDE5 inhibitors to treat BPH, while the specification only identifies a few example PDE5 inhibitors. Third, Lilly argues that the '124 patent lacks support for the negative claim limitation in claim 1.

Lilly's first argument is unsupported by the law or the facts, which demonstrate that the '124 patent specification clearly disclosed using inhibitors of PDE5 to treat BPH. And Lilly waived this argument by not raising it in a Rule 50(a) motion. Lilly's second and third arguments simply rehash legal issues this Court has already decided in UroPep's favor. The Court should deny Lilly's motion for JMOL or a new trial on written description.

A. Legal Standard

In order to satisfy the written description requirement, "the description must 'clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'" *Ariad Pharm. Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (alteration in original)). "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "[D]etermining whether a patent complies with the written description requirement will necessarily vary depending on the context. . . . For generic claims, we have set forth a number of factors for evaluating the adequacy of the disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" *Id.* (quoting *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005)). The court "must accord deference to the jury findings on written description," because written description is "intensely factual" and not amenable to "wooden rules." *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000) (citations and quotations omitted).

B. Claim 1 Of The '124 Patent Is Not Too Narrow: The Specification Describes PDE5 Inhibitors To Treat BPH

Lilly first argues that claim 1 of the '124 patent is invalid because it is too narrow. Lilly argues that (1) the specification does not support a claim directed to an inhibitor of only PDE5, and not also PDEs 1 and 4; and (2) the specification does not adequately describe treating just BPH, as opposed to other prostatic diseases mentioned in the specification. Lilly Br. at 12-15.

Lilly's challenge to the narrowness of claim 1 is unsupported by the record and, as discussed further below, Lilly waived the argument by failing to raise it in its Rule 50(a) motion during trial. The '124 patent specification repeatedly refers to using inhibitors of PDEs 1, 4, *or* 5. *See e.g.*, Dkt. 177-1, '124 patent col. 4, ll. 65-68 ("In the preparation of medicaments . . . an effective amount of the inhibitors of sPDE I, IV, or V..."); *id.* at col. 7, ll. 35-38 ("[A] compound is suitable for the purpose according to the invention, i.e., is an inhibitor of sPDE I, IV, or V..."). The specification then lists, as "preferred selective inhibitors of PDEI, IV, and V," several compounds that a person of skill in the art would have recognized as selective inhibitors of PDE5, including sildenafil, zaprinast, E4021, and MY5445. *Id.* at col. 2, l. 28 – col. 4, l. 44. *See also* Ex. A, Tr. at 514:24-515:4 (Dr. Roehrborn testifying that sildenafil and zaprinast are "PDE5 inhibitors disclosed in the '124 patent"); *id.* at 511:11-24 (Dr. Roehrborn discussing sildenafil as a "selective inhibitor of cGMP"); *id.* at 1259:1-21; 1260:24-1261:14 (Dr. Bell discussing Eisai compounds that are potent and selective PDE5 inhibitors, including E4021, which is compound "d" in the specification); Dkt. 190-6, Trial Ex. 242, Takase 1993, at 2 (showing the selectivity of MY5445). Similarly, the specification identifies BPH as a particularly relevant disease to be treated with these inhibitors. Dkt. 177-1, at col. 2, ll. 17-20 ("[T]he subject matter of the invention is the use of specific inhibitors of sPDE I, sPDE IV and sPDE V in the prophylaxis and treatment of prostatic diseases, in particular, benign prostatic hyperplasia....").

The '124 patent specification describes treating BPH or other prostatic diseases with inhibitors of PDE1, PDE4, or PDE5, and provides specific examples of known selective PDE5 inhibitors that could be used in the invention. Claim 1 focuses on one of the most prominently disclosed alternatives – using PDE5 inhibitors to treat BPH. It is axiomatic that a patent can claim a subset of what is described in the specification, leaving the remainder of the invention to the public. *See, e.g., Miller v. Bridgeport Brass Co.*, 104 U.S. 350, 352 (1881) (“[T]he claim of a specific device or combination, and an omission to claim other devices or combinations apparent on the face of the patent, are, in law, a dedication to the public of that which is not claimed.”). That the inventors targeted their claims to inhibitors of one of the three PDEs described in the specification does not render the claims invalid. *See Snitzer v. Etzel*, 465 F.2d 899, 902-03 (C.C.P.A. 1972) (holding written description adequate, in a nascent field, where the claim focused on 1 of 14 possible ions listed in the specification, noting that “the literal description of a species provides the requisite legal foundation for claiming that species”). *See also In re Driscoll*, 562 F.2d 1245, 1250 (C.C.P.A. 1977) (written description requirement met where, like here, “the exact subgenus claimed [wa]s clearly discernible in the generalized formula”).

Moreover, this Court has already rejected the notion that the '124 patent's silence on the benefits of inhibiting PDE5 versus PDEs 1 or 4 renders the claim invalid as a matter of law. In its order denying Lilly's motion for summary judgment of no written description, the Court noted “that the '124 patent does not describe . . . why a person of ordinary skill would single out PDE V rather than the other two PDE inhibitors [sic] of interest, PDE I and PDE IV.” Dkt. 149, Mem. Op. & Order at 35. But the Court held that whether this and other “omissions from the specification . . . render the specification insufficient to provide the necessary written description of the inventions of the '124 patent is a factual issue.” *Id.* at 37. The jury resolved that factual

issue in UroPep's favor (in part because no Lilly witness testified about this and Lilly never argued it, which is proof it was waived). Lilly presents no reason to disturb the jury's findings.¹

The cases Lilly cites provide no support for its argument. Lilly first cites *In re Ruschig*, 379 F.2d 990 (Fed. Cir. 1967), which involved a patent claiming novel compounds. *See* Lilly Br. at 12-13. The specification in *Ruschig* generally described parameters covering over half a million compounds, but did not specifically list the claimed compound or include other information that would have guided someone to the claimed compound.² *In re Ruschig*, 379 F. 2d at 993-94. Here, the relevant choice is between inhibitors of three PDEs – PDE1, PDE4, and PDE5 – not a half-million options like in *Ruschig*. Further, the specification here explicitly discloses using “medicaments” containing “an effective amount of the inhibitors of sPDE I, IV, *or* V,” Dkt. 177-1, '124 patent col. 4, ll. 65-68 (emphasis added), and specifically calls out BPH as one of the particular prostatic diseases that could be treated using this invention, *id.* at col. 2, ll. 17-20. Finally, unlike *Ruschig*, in which a claim was added to cover a newly-discovered compound, the parties agree that tadalafil was known to a person of ordinary skill as a selective PDE5 inhibitor. *Ruschig* does not support Lilly's position.

¹ To support its invalidity case, Lilly argues that the invention's lack of focus “on use of a selective PDE V inhibitor alone to treat just BPH is manifest from the claims, which . . . claimed generic methods of treating all disclosed conditions with any of the specifically disclosed compounds.” Lilly Br. at 7. (citing Dkt. 106-4, '061 File History, at JX_061_FH0024-35). Lilly ignores that the “specifically disclosed compounds” included PDE5 inhibitors, such as sildenafil, zaprinast, E4021, and MY5445. Further, the claims cited by Lilly recite treating a variety of conditions – including, “in particular benign prostatic hyperplasia.” *See* Dkt. 106-4 at JX_061_FH0024. If anything, this history further supports that, at the time of the original filing, the inventors were in possession of the claimed invention – the use of a PDE5 inhibitor to treat BPH.

² The specification in *Ruschig* included a table listing some examples, including one similar to the claimed compound. *Id.* at 995. But the court held that a similar example is not sufficient. *Id.*

Lilly also cites *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336 (Fed. Cir. 2013), arguing that it “compels the invalidity of claim 1 of the ’124 patent.” Lilly Br. at 13. It does not. In *Novozymes*, the patent claimed novel enzymes with certain characteristics, but the original specification provided “only generalized guidance listing several variables that might, in some combination, lead to a useful result.” 723 F.3d at 1346. The court found the claim invalid in large part because the application “contain[ed] no disclosure of any variant that actually satisfie[d] the claims, nor [wa]s there anything to suggest that Novozymes actually possessed such a variant at the time of filing.” *Id.* at 1348. *See also id.* at 1349 (“[O]ne searches the [patent] application in vain for the disclosure of even a single species that falls within the claims or for any ‘blaze marks’ that would lead an ordinarily skilled investigator toward such a species among a slew of competing possibilities.”). In contrast, the ’124 patent does not claim novel PDE5 inhibitors; it claims a novel method of treating BPH with a PDE5 inhibitor. Moreover, the patent lists several example compounds that could be used in the claimed invention, and hundreds of other inhibitors were known at the time to a person of ordinary skill in the art. *See Ex. A, Tr.* at 1254:21-25 (“There were hundreds of selective inhibitors known by July, 1997.”); *id.* at 1257:12-1259:21; 1272:2-1273:8; 1273:23-1274:4 (discussing some of the hundreds of selective PDE5 inhibitors that were known to a person of ordinary skill at the time). *Novozymes* is not this case.³

³ In an attempt to bring this case closer to *Novozymes*, Lilly wrongly asserts that, “[a]s in *Novozymes*, the purported invention of the ’124 patent was incomplete Dr. Ückert himself characterized the ‘work’ that the inventors allegedly did and disclosed in the patent as a ‘research plan.’” Lilly Br. at 14 (citing Ex. A, Tr. at 162:3-15). But the testimony Lilly cites concerned the “research plan” that preceded the invention described in the patent; Lilly cites no testimony from Dr. Ückert in which he agreed that the patent itself merely discloses a research plan.

The other cases Lilly cites are similarly inapposite. *See Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1358, 1364 (Fed. Cir. 2011) (affirming summary judgment of invalidity of claim to “drug-eluting stents utilizing ‘rapamycin, or a macrocyclic lactone analog thereof’ as the therapeutic agent,” where the specification disclosed no such analogs and the patentee admitted the field was in its infancy at the time of application); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) (affirming denial of motion to add a sub-genus count to an interference claiming a novel sub-genus that “diverge[d] from [the specification’s] preferred elements at least with respect to position R,” and the specification provided “no indication that position R would be a better candidate for substitution than any other”).

Finally or first, as the Court wishes to decide this issue, Lilly did not raise its narrowness challenge to claim 1 “in its pre-verdict Rule 50(a) motion for judgment as a matter of law. [Lilly] has therefore waived the right to make that argument as part of its renewed motion for judgment as a matter of law under Rule 50(b).” *Bianco*, 2014 WL 5462388, at *6 (citations omitted).

Lilly’s Rule 50(a) motion on written description focused only on the allegedly impermissible breadth of the claim:

MR. VARE: The Rule 50 motion would be also on written description, that the evidence meets the clear and convincing evidentiary standard to show that the inventors did not possess the full scope of the claim.

Ex. A, Tr. at 1392:11-14. Lilly’s Rule 50(a) motion never mentioned Lilly’s challenge to the narrowness of the claim; it was focused only on whether the inventors possessed “the full scope of the claim.” Moreover, Lilly’s challenge to the “narrowness” of claim 1 did not feature at all in its trial presentation. Accordingly, neither the Court nor UroPep could have been expected to understand that this was a basis for Lilly’s Rule 50(a) motion.

C. Claim 1 Of The '124 Patent Is Not Too Broad: The Patent Describes Using An Effective Amount Of A PDE5 Inhibitor To Treat BPH

After arguing that claim 1 is too narrow, Lilly next argues it is too broad. *See* Lilly Br. at 15-25. Lilly's brief rehashes the arguments that this Court rejected at the summary judgment phase. *See* Dkt. 149, Mem. Op. & Order at 27-37. And Lilly persists in making the same fundamental errors here that it made at summary judgment – mischaracterizing the '124 patent as an invention of novel compounds and ignoring the advanced state of the art at the time of the invention. This Court has already found that the '124 patent claims “are directed to the use of PDE V inhibitors to treat BPH, not to the discovery of PDE V inhibitors themselves,” *id.* at 30, and that “there were hundreds of known PDE V inhibitors” at the time of the invention, *id.* at 31. Thus, in this case, “the written description issue does not turn on whether the patentees were in possession of the entire genus of PDE V inhibitors.” *Id.* at 30. Instead, “the written description requirement is satisfied if the specification shows that the inventors possessed the method of treating BPH by administering an inhibitor of PDE V.” *Id.* at 31.

Applying the correct inquiry, substantial evidence supports the jury's conclusion that the '124 patent inventors were in possession of the claimed invention – the use of PDE5 inhibitors to treat BPH. Both the field of PDE5 inhibitors, and the field of medications for treatment of BPH, were well developed by July 1997 (though, of course, no one had put those two fields together before the inventors of the '124 patent). *See, e.g.,* Ex. A, Tr. at 318:11-18 (“state of the art” of “PDE5 inhibitors” was “very well developed” by July 1997); *id.* at 491:20-492:12 (Dr. Roehrborn testifying that, by July 1997 “80, 90 percent of the patients received an alpha blocker”); *id.* at 1295:20-1296:2 (discussing “what was already known about treating BPH with other medications, not PDE5 inhibitors”). The parties' experts agreed that over a hundred PDE5 inhibitors, including tadalafil, were known to a person of ordinary skill in 1997. *See, e.g.,* Ex. A,

Tr. at 341:19-22 (UroPep expert Dr. Bell agreeing that “hundreds of PDE5 inhibitors were known before 1997”); *id.* at 792:7-17 (Lilly expert Dr. Rotella agreeing that tadalafil and over a hundred other PDE5 inhibitors were known in 1997). Moreover, by the time of the ’124 patent’s invention, two PDE5 inhibitors – sildenafil and zaprinast – had been subjected to human clinical testing. *Id.* at 1293:24-1294:3. And, although Lilly’s expert disagreed, Dr. Bell testified that, given “what was already known about treating BPH with other medications, not PDE5 inhibitors,” only “routine” experimentation would have been needed to implement the ’124 patent’s invention in July 1997. Ex. A, Tr. at 1295:20-1296:2. *See also id.* at 1294:4-17 (Dr. Bell testifying that determining an “effective amount of a PDE5 inhibitor” would have required a person of ordinary skill in 1997 to engage in merely “routine dose ranging”).

On top of all of this existing knowledge, the ’124 patent describes human tissue strip testing that demonstrated the efficacy of using PDE5 inhibitors to relax prostatic smooth muscle. ’124 patent col. 7, ll. 14-34. *See also* Dkt. 149, Mem. Op. & Order at 34-35 (discussing the disclosure in the ’124 patent). The patent also provides detailed protocols for testing the potency and selectivity of PDE5 inhibitors, and discusses how PDE5 inhibitors work to relax prostatic smooth muscle. *See* Ex. A, Tr. at 316:18-317:8 (Dr. Bell testifying that the ’124 patent describes more experimentation than Pfizer conducted around that time to identify PDE5 inhibitors). The experiments described in the patent could be used to measure the potency and selectivity of a given PDE5 inhibitor and, using those tests, a person of ordinary skill could determine whether a given inhibitor would be effective to treat BPH. *See id.* at 1296:13-23 (Dr. Bell affirming that the ’124 patent has enough information to “guide a person regarding how to determine whether a clinical candidate or compound is effective as a PDE5 inhibitor,” and noting that the ’124 patent “tells us how to run IC50 assays and how to confirm those IC50 assays in a tissue strip

experiment”). In light of the advanced state of the art, the UroPep inventors’ disclosure of four selective PDE5 inhibitors and detailed teachings on how to identify and test additional candidates, is more than enough to satisfy the written description requirement.⁴

The Court adopted the key part of Lilly’s proposed instruction on written description, and instructed the jury that the patent must include “a sufficient number of representative compounds or a common structural feature, such that a person of ordinary skill in the art would understand, from reading the patent, that the inventor invented the full scope of the claimed method.” *See* Dkt. 333, Final Jury Instr at 16. *See also* Dkt. 326, Lilly Mot. re Written Description Instr. at 2. The jury found that, given the state of the art and the disclosure in the patent, the example compounds in the patent are enough to demonstrate that the inventors had possession of the claimed invention. Lilly has presented no reason to undo the jury’s findings.

1. Lilly’s Critique Of The Number Of Potential Compounds That Could Be Used In The Invention Is Misplaced

Lilly expends a great deal of effort criticizing the inventors of the ’124 patent for not listing a sufficient number of representative PDE5 inhibitors. The word “billions” (as in billions of compounds) appears more than ten times in Lilly’s brief. *See* Lilly Br. at 4, 9, 15-16, 18-19,

⁴ Dr. Bell’s testimony regarding common structural and physical features of PDE5 inhibitors further supports the jury’s written description verdict. *See* Ex. A, Tr. at 1259:22-1263:5; 1264:12-23; 1280:10-1281:7. Lilly argues that the “frog” structure shared by a number of PDE5 inhibitors, including a number of compounds in the ’124 patent and tadalafil, cannot support written description because it is not common to all PDE5 inhibitors, and is also shared with other types of inhibitors. *See* Lilly Br. at 22-23. Lilly ignores that Dr. Bell elaborated on the “frog” testimony, explaining that, while not all PDE5 inhibitors share the exact same frog-like structure, they do all share common physical features that impact “the way they fit into this active site that we talked about in the PDE5.” Ex. A, Tr. at 1280:10-1281:7. In any case, Lilly did not object at trial to any of this testimony, and the attacks Lilly now raises are precisely the sorts of issues that Lilly could have chosen to explore in front of the jury.

31-34. Lilly argues that given the large number of compounds that could potentially be used in the invention, the example selective PDE5 inhibitors listed in the patent do not suffice.

Lilly's focus on the ratio between the number of potential compounds that could be used in the invention and the number of compounds disclosed in the specification completely ignores that a person of ordinary skill would have been aware of hundreds of other PDE5 inhibitors. This is a deliberate mistake about the law Lilly has made before. "A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before." *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (internal citation omitted). The Court noted this exact problem with Lilly's argument in its summary judgment ruling. *See* Dkt. 149, Mem. Op. & Order at 36-37 (noting that "[i]t was not necessary for the patentee to include in the specification a catalogue of all then-known PDE V inhibitors").

Lilly incorrectly suggests that the '124 patent would have somehow been saved by recopying that which was common knowledge into the specification. Lilly Br. at 15-21. As the Federal Circuit explained in the context of DNA patents, § 112 does not require a patent to "recite known [] structures," as that "would only add unnecessary bulk to the specification. . . . [W]here, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences, . . . satisfaction of the written description requirement does not require either the recitation or incorporation by reference . . . of such genes and sequences." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006). Here too, a laundry-list of known PDE5 inhibitors would add "unnecessary bulk" to the specification and would "neither

enforce the quid pro quo between the patentee and the public by forcing the disclosure of new information, nor would it be necessary to demonstrate to a person of ordinary skill in the art that the patentee was in possession of the claimed invention.” *Id.*

“The appropriate number of species that one must disclose when claiming a genus ‘necessarily changes with each invention, and it changes with progress in a field.’” *Boston Sci.*, 647 F.3d at 1363 (quoting *Ariad*, 598 F.3d at 1350). The jury heard substantial evidence about the advanced state of the field of PDE5 inhibitors in July 1997 and the large number of inhibitors that would have been known to a person of ordinary skill at the time. The jury was free to credit that evidence and conclude that the written description requirement had been satisfied. *See In re Herschler*, 591 F.2d 693 (C.C.P.A. 1979) (upholding the validity of a claim to topically administering a steroid together with a solvent, where the specification only disclosed one example steroid, because numerous other steroids were known at the time and the novelty of the claim was administering steroids with the claimed solvent, not novel steroids).⁵ *See also In re Fuetterer*, 319 F.2d 259 (C.C.P.A. 1963) (holding valid a claim to a combination of substances that includes certain inorganic salts where the specification only listed four examples of such salts, because the novelty of the invention was the combination).

Like in its summary judgment motion, Lilly’s attack on the over-breadth of the ’124 patent is based on inapposite cases dealing with inventions claiming novel compounds in nascent

⁵ Lilly argues that later Federal Circuit cases have confined *Herschler* to circumstances where the relevant class of compounds are “chemically similar.” *See* Lilly Br. at 23-25. Not so. The key feature distinguishing *Herschler* from many other Federal Circuit cases is the nature of the invention and the state of the art at the time of the invention. For example, in *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916 (Fed. Cir. 2004), the court focused on the fact that the invention in *Rochester* was to a novel class of compounds, while in *Herschler* the novelty was the use of a DMSO solvent, and “numerous physiologically active steroidal agents were known to those of ordinary skill in the art.” *Id.* at 928. *See also* Dkt. 149, Mem. Order & Op. at 30-33 (discussing *Herschler*, *Fuetterer*, *Rochester*, and *AbbVie*).

fields. For example, in *Boston Scientific*, one set of patents claimed “drug-eluting stents utilizing rapamycin, or a macrocyclic lactone analog thereof.” *Boston Sci.*, 647 F.3d at 1358 (quotation omitted). But the patents “contain[ed] no examples of macrocyclic lactone analogs of rapamycin, and g[a]ve no guidance on how to properly determine whether a compound is a macrocyclic lactone analog of rapamycin besides vaguely indicating they must be ‘structural[ly] similar’ to rapamycin.” *Id.* at 1365. Moreover, while “some species of this vast genus were known in the art” at the time, “very little knowledge existed regarding the use of drug-eluting stents” for purposes like those described in the patent, and the patentee agreed “that the state of the art was highly unpredictable.” *Id.* at 1364-65. The other patent at issue in *Boston Scientific* claimed “‘rapamycin or a macrocyclic triene analog thereof’ in combination with specific drug-eluting stents.” *Id.* at 1367. But the specification “fail[ed] to disclose even a single member of either genus of ‘analog’ of rapamycin, or the more specific genus of ‘macrocyclic triene analogs.’” *Id.* And the claimed technology “was still in its infancy” at the time of the effective filing date of the patent. *Id.* In contrast, the field of PDE5 inhibitors was very advanced in July 1997, and the use of oral medications to treat BPH was well known.

Lilly relies heavily on *Ariad*, arguing that it goes “directly to the point” that disclosing one specific compound cannot support a claim to an entire genus. *See Lilly Br.* at 25. *See also id.* at 15 (arguing that the ’124 patent claims fail the *Ariad* “line of cases”). Lilly ignores that, in *Ariad*, “[t]he state of the art at the time of filing was primitive and uncertain.” 598 F. 3d at 1358. The claims in *Ariad* were directed to “three classes of molecules potentially capable of reducing Nf-kB activity.” *Id.* at 1355. But the prior art at the time did not contain a single example inhibitor of Nf-kB. *Id.* at 1356-57. And the only examples listed in the patent (by the relevant priority date) had not been shown to actually inhibit Nf-kB. *Id.* In contrast, Lilly’s expert

admitted that more than 100 PDE5 inhibitors were known in the art at the time of the '124 patent's priority. And the evidence shows that the state of the art at the time was well-developed. The so-called "*Ariad* line of cases" provide no support for Lilly's argument that the '124 patent claims are invalid. *See also Centocor Ortho Biotech, Inc. v. Abbott Labs*, 636 F.3d 1341 (Fed. Cir. 2011) (claims covering fully-human antibodies lacked written description where no such antibodies were known and the specification did not describe any fully-human antibodies); *In re Alonso*, 545 F.3d 1015 (Fed. Cir. 2008) (patent covering a large and diverse genus of antibodies lacked sufficient written description where patent only disclosed one species and the court cites no evidence that other species would have been known to a person of ordinary skill in the art).

2. Lilly's Additional Critiques Relating To The Number Of Example Compounds Are Incorrect And Irrelevant

Predictability: Lilly argues that the number of potential PDE5 inhibitors is particularly problematic because of the difficulty in predicting and determining which would work in the invention. *See Lilly Br.* at 16-19. But Dr. Bell testified as follows about the ease and speed with which Pfizer could screen its 500,000-compound collection:

Q. And could Pfizer screen those compounds very quickly?

A. Yes. They did it routinely. So, at that time we could screen the entire Pfizer collection in two or three weeks.

Q. And, Dr. Bell, was that unique to Pfizer or in July of 1997 was screening like that quite common?

A. It was -- I think it was commonplace. The method -- the technology was available to every pharmaceutical company and I'm pretty sure that most did.

Q. So, Dr. Bell, if there were millions of quinazolines in the library, would it take very long to screen them with high throughput screening?

A. No, it wouldn't. As I said, it would take roughly two to three weeks to complete that high throughput screen, although we

personally didn't do it on PDE5 in 1997. I think we did it in 1999; so -- because we already had sildenafil; but we went back and screened our collection in 1999.

Ex. A, Tr. at 1282:14-1283:7. Dr. Bell also confirmed that “all compounds able to inhibit PDE5 can work to treat BPH provided they are potent enough to be delivered in effective quantities.”

Id. at 334:12-15.⁶ Thus, after screening the compounds for their inhibitory effect, a person of ordinary skill would have been ready to determine which could be used in the claimed invention.

Lilly's expert disagreed with Dr. Bell, stating that, even with potency and selectivity data, it would be impossible to predict “whether a compound could be used to treat a disease.” *Id.* at 857:8-12. But Lilly's expert admitted that his own PDE5 inhibitor patent covered possibly millions of compounds, and yet provided “no potency or selectivity data.” *Id.* at 857:13-20. The jury was free to disregard testimony that was inconsistent with Lilly's expert's own prior practices.

Diversity of potential PDE5 inhibitors: Lilly repeatedly asserts that PDE5 inhibitors are “diverse.” *See, e.g.,* Lilly Br. at 2, 4, 16, 18, 21-22, 30. As will be discussed below, a person of skill would have recognized important structural similarities between PDE5 inhibitors.

Exclusion of tadalafil: Lilly also argues that, based on the *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285 (Fed. Cir. 2014) case, the '124 patent lacks a written description because it does not list tadalafil as an example compound. *See* Lilly Br. at 21. Lilly describes the omission of tadalafil as “critical.” *Id.* at 20. Lilly ignores the significant differences between the omission of tadalafil from the '124 patent and the omissions at issue in

⁶ Lilly incorrectly asserts that “Dr. Bell admitted that a person of skill in the art would not know whether zaprinast . . . would be effective in treating BPH without testing it.” Lilly Br. at 18-19. In fact, the cited testimony from Dr. Bell was only that he did not know whether “10 milligrams of zaprinast would be effective” Ex. A, Tr. at 338:23-339:9. Lilly overstates the record.

AbbVie. The patent in *AbbVie* was directed to “new compositions, *i.e.*, fully human antibodies having desired IL-12 binding characteristics.” *AbbVie*, 759 F. 3d at 1301. And, in *AbbVie*, there was “no evidence to show whether one of skill in the art could make predictable changes to the [patent’s] described antibodies to arrive at other types of antibodies such as [the accused antibody].” *Id.* But in this case, the evidence is undisputed that a person of skill in the art at the time would have known that tadalafil is a selective PDE5 inhibitor and thus could be used to practice the claimed invention. Further, the ’124 patent does not claim any new compositions. Rather, it claims a new use for an existing set of compositions. *AbbVie* is inapposite.⁷

Lilly’s misplaced focus on the number of compounds in the specification would also lead to absurd results. As Lilly’s expert testified, under its view of the written description requirement, an “enormous” number of compounds would need to be listed in the patent, and “it would be effectively impossible” to adequately support a claim like claim 1 of the ’124 patent. *See Ex. A, Tr. at 755:17-756:6.* Lilly’s approach would also upend the settled expectations of the pharmaceutical industry and invalidate numerous existing patents, including many Lilly patents. *See Dkt. 129, UroPep Opp’n To Lilly SJ Mots. at 35-40* (discussing Lilly’s and others’ patents covering the use of diverse classes of compounds like NSAIDs, CYP2D6 inhibitors, and PDE5 inhibitors); *Dkt. 130-5, List of Eli Lilly Patents with Claim Term “Inhibitor.”*

3. A Person Of Ordinary Skill Would Have Recognized Common Structural Features Of PDE5 Inhibitors

The ’124 patent also satisfies the written description requirement because the PDE5 inhibitors disclosed in the specification share common structural features with the other,

⁷ *AbbVie* is also procedurally inapposite, as it involved the Federal Circuit’s review of a denial of JMOL after a jury found a patent invalid for lack of written description. The court was thus compelled in that case to view the facts in the light most favorable to the party challenging the validity of the patent. The opposite is true here.

undisclosed PDE5 inhibitors, including tadalafil. Dr. Bell testified that many of the PDE5 inhibitors known at the time, including both tadalafil and E4021 – a compound disclosed in the ’124 patent specification – shared a common “benzodioxole” or “methylenedioxy” group. Ex. A, Tr. at 1259:22-1260:8; 1261:23-1262:12. This frog-like structure “is important to the PDE5 binding” of these compounds. *Id.* at 1260:14-18. Finally, Dr. Bell agreed that “a skilled person in 1997” would understand that this structure “would be important to the binding of tadalafil with PDE5 just like it is with the Eisai compounds.” *Id.* at 1263:2-5. None of this testimony was contradicted by Lilly’s experts, who did not discuss this common structural feature.

While it is true that not all PDE5 inhibitors share the “frog” structure, they do all share common physical features that impact “the way they fit into this active site that we talked about in the PDE5.” *Id.* at 1279:17-1281:7. Dr. Bell explained that this common physical shape resembles an “envelope,” with a “flat bit then (demonstrating) a flap going up.” *Id.* And Lilly’s own expert agreed that he did not identify any evidence that tadalafil, sildenafil, or “any of the listed compounds in the ’124 patent bind differently to PDE5.” *Id.* at 794:16-795:4.

Lilly did not object to, or rebut, the evidence that a person of ordinary skill in the art would have recognized important structural similarities shared by PDE5 inhibitors.⁸ Lilly had ample opportunity to explore this issue with Dr. Bell; the first few minutes of Lilly’s cross-examination were focused on this issue. *See id.* at 1298:17-1302:3. “To the extent [Dr. Bell’s] credibility, data, or factual assumptions have flaws, these flaws go to the weight of the evidence, not to its admissibility. . . . [D]isputes over the expert’s credibility or over the accuracy of the

⁸ Lilly’s failure to object to this evidence at trial waives any evidentiary objections to Dr. Bell’s testimony about the structural similarities shared by PDE5 inhibitors. *See Fed. R. Civ. P.* 103(a); *see also Wilson v. Waggener*, 837 F.2d 220, 222 (5th Cir. 1988) (“In order to preserve the admission of evidence as error for appellate review, an objection must be made at trial.”).

underlying facts are for the jury.” *Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1299 (Fed. Cir. 2015). Lilly has presented no compelling reason to disregard the jury’s findings.

D. The Negative Claim Limitation Is Supported By The Specification’s Description Of Alternative PDE5 Inhibitors

Lilly’s proposed negative limitation instruction, and its post-trial attack on the negative claim limitation, incorrectly suggest that the specification must provide a reason to exclude that goes beyond clearly enshrining the patentee’s choice to claim less than the full scope of the invention described in the specification. No such explanation is required; a patentee is free to claim whatever portion of the invention that the patentee chooses to claim, so long as the scope of what is claimed is clear and does not contradict any portion of the specification.

The ’124 patent claims the use of any one PDE5 inhibitor to treat BPH, other than a compound drawn from a list of eight compounds. The specification identifies several example compounds that could be used in the invention. *See* Dkt. 177-1, col. 2, l. 28 – col. 4, l. 44. The patent further provides examples where a single PDE5 inhibitor – sildenafil – is administered by injection or by topical administration. *Id.* at col. 6, l. 65 – col. 7, l. 10. And the specification explains how to determine whether “a compound is suitable for the purpose according to the invention....” *Id.* at col. 7, ll. 35-36. The specification thus describes the invention of using any one PDE5 inhibitor capable of being administered in an effective amount to treat BPH. The inventors were free to claim less than this full invention.

In *In re Johnson*, 558 F.2d 1008, 1013 (C.C.P.A. 1977), the patent office rejected a claim to a genus of polymers that excluded, without explanation, two species falling within that genus. The patent office “found that ‘no antecedent basis exists in the parent case’ for the ‘limited genus’ in claim 1,” and therefore rejected the claim for lack of written description. *Id.* at 1018.

The court reversed, holding that the original specification clearly described the entire genus, and by definition therefore also described that genus minus two species. *Id.* As the court explained:

The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of s 112, first paragraph, appears to result from a hypertechnical application of legalistic prose

Id. at 1019. The court also noted that the reason for the applicant’s exclusion of those two species was evident from the prosecution history, which was “properly presented and relied on” to provide context for the exclusion. *Id.* The court in *Johnson* never suggested that this context was necessary to salvage the claim; to the contrary, nothing more than a clear explanation of the scope of the claim was required. So too here, nothing more than clearly describing alternative species that could be used in the invention was required to support this claim. *See also Inphi Corp. v. Netlist, Inc.*, 805 F.3d 1350, 1357 (Fed. Cir. 2015) (holding that there is no “heightened written description standard for negative claim limitations and that properly described, alternative features are sufficient to satisfy the written description standard of § 112, paragraph 1 for negative claim limitations”); Dkt. 328, UroPep Submission re Negative Claim Limitation Jury Instr *But cf. In re Bimeda Research & Dev. Ltd.*, 724 F.3d 1320 (Fed. Cir. 2013) (claim excluding only one antiinfective not adequately supported by specification that described “antiinfective free” applications).

Further, the history of the ’124 patent provides ample explanation for the compounds excluded from the ’124 patent. As the Court noted, certain compounds were excluded to avoid a double-patenting rejection. *See* Dkt. 359, Mem. Op. at 11. In the end, these exclusions were not necessary because the inventors filed a terminal disclaimer. *See* Ex. B, Trial. Ex. 194, ’124 File

History, at JX_124_FH0241. But the inventors initially sought to overcome the double-patenting rejection by excluding the compounds in the '061 patent from the scope of the claim. *Id.* at JX_124_FH0217-19. They chose not to exclude zaprinast because they had previously elected zaprinast as the species to be considered by the patent office.⁹ *Id.* at JX_124_FH0096. While not necessary to describe the negative claim limitation, this context provides further support for the Court's rejection of Lilly's request for a negative claim limitation instruction.

V. ENABLEMENT

Lilly's enablement motion is premised on the same fundamental misunderstanding of the nature of the '124 patent that infects its written description arguments. Lilly proceeds on the mistaken belief that the '124 patent covers all PDE5 inhibitors. On the basis of that mistaken belief, Lilly asserts that UroPep has not enabled the full scope of the claim because the identification and synthesis of every PDE5 inhibitor would require undue experimentation. But the '124 patent does not claim all PDE5 inhibitors. As this Court has already recognized, the '124 patent claims "are directed to the use of PDE V inhibitors to treat BPH, not to the discovery of PDE V inhibitors themselves." Dkt. 149, Mem. Op. & Order at 30. The full scope of claim 1 is enabled because the patent teaches that sufficiently potent and selective PDE5 inhibitors can be used to treat BPH, identifies example selective PDE5 inhibitors that can be used in the invention, and teaches a person of skill in the art how to determine whether any given PDE5 inhibitor can work in the invention. In light of the maturity and predictability of the relevant

⁹ The inventors likely thought that excluding zaprinast was not necessary to overcome the double patenting rejection because zaprinast is listed in claim 3 of the '061 patent, which claims a method of "relaxing prostatic muscles," and is not listed in claim 1, which claims a method of "treating . . . benign prostatic hyperplasia." Dkt. 106-2, '061 Patent, at 6. *See also* Ex. B, Trial Ex. 194, '124 File History, at JX_124_FH0221 (explaining that the negative limitation "excludes from the present claims every compound . . . recited in the patented claims for "treating . . . benign prostatic hyperplasia").

field, nothing more is necessary to enable the full scope of this claim. Moreover, even if the Court accepts Lilly's understanding of the enablement requirement here, the jury was free to conclude that Lilly failed to provide clear and convincing evidence that claim 1 is not enabled.

“Whether making and using an invention would have required undue experimentation, and thus whether a disclosure is enabling under 35 U.S.C. § 112, ¶ 1 (1994), is a legal conclusion based upon underlying factual inquiries.” *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1354 (Fed. Cir. 1998) (citing *In re Wands*, 858 F.2d 731, 735, 736-37 (Fed. Cir. 1988)). *See also Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1376-77 (Fed. Cir. 2007) (defendant failed to satisfy “the heavy burden required to overturn the jury’s verdict[]” that the patent met the enablement requirement because “[t]he jury was free to credit” expert testimony that “a person of skill in the art would be fully enabled to practice the invention based on the specification’s disclosure”).

“Because we must presume a patent enabled, the challenger bears the burden, throughout the litigation, of proving lack of enablement by clear and convincing evidence. . . . [T]here is no formal burden-shifting framework when addressing the issue of enablement.” *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1337-38 (Fed. Cir. 2013).

A. The *In re Wands* Factors Show That Claim 1 Of The '124 Patent Is Enabled

In *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the Federal Circuit set forth eight factors “to be considered in determining whether a disclosure would require undue experimentation” Lilly identifies the eight *Wands* factors, Lilly Br. at 28, but never explains why it believes those factors support its enablement challenge. An examination of those factors supports the jury’s conclusion that claim 1 of the '124 patent is enabled.

1. The Quantity of Experimentation Necessary

Dr. Bell's testimony shows that the amount of experimentation necessary to screen for the selectivity and potency of a PDE5 inhibitor is quite minimal. For example, he testified that, using technology that "was available to every pharmaceutical company" at the time, Pfizer's entire collection of "about 500,000" PDE5 inhibitors could be screened for selectivity in two or three weeks. Ex. A, Tr. at 1282:2-23.

Dr. Bell also testified that a person of ordinary skill in the art would have been familiar with the patent's disclosed methods for testing the selectivity and potency of PDE5 inhibitors. *See id.* at 1284:7-16 (testifying that the methods disclosed by Galwan and Nicholson, and referenced in the '124 patent, were "commonly used throughout the industry").

Given the knowledge of a person of ordinary skill, the '124 patent taught a person of ordinary skill how to practice the full scope of the claimed invention. As Dr. Bell testified:

Q. I want to focus you on what was already known about treating BPH with other medications, not PDE5 inhibitors.

Do you believe, based on that and the known PDE5 inhibitors that we talked about today, undue experimentation would have been necessary to use the invention in July 1997?

A. No. I think it would have been routine.

Q. And just to put that in a concrete example, would the work required to use the '124 invention with a known PDE5 inhibitor like zaprinast have been routine or difficult and unreasonable?

A. I think it would have been a routine clinical experiment.

Q. Given the knowledge of a person of skill in 1997, did the patent present sufficient direction or guidance to practice the claims?

A. Yes, I think it does.

Id. at 1295:20-1296:12.

Dr. Bell further explained that “all compounds able to inhibit PDE5 can work to treat BPH provided they are potent enough to be delivered in effective quantities.” *Id.* at 334:12-15. Further, once a potent, selective PDE5 inhibitor is identified with these screening methods, its clinical development requires only “routine” or “normal” clinical experimentation. *Id.* at 1293:9-23. *See also id.* at 922:3-18, 949:6-18 (Dr. Viktrup discussing the “normal course of drug development” that Lilly followed to clinically develop tadalafil); *id.* at 1294:4-17 (Dr. Bell testifying that determining an “effective amount of a PDE5 inhibitor” would have required a person of ordinary skill in 1997 to engage in merely “routine dose ranging”); *id.* at 1298:3-10 (there has never been a potent PDE5 inhibitor that “has been dose-range studied” that has been ineffective in treating BPH). The patent’s disclosures, combined with what was already known by a person of skill in the art, provided all the information needed to practice the invention.

Lilly sets-up a straw man, arguing that the amount of experimentation needed to practice the full scope of the claims is “undue” because it would require the synthesis, screening, and development of billions of compounds. *See Lilly Br.* at 31-35. But claim 1 of the ’124 patent does not claim every PDE5 inhibitor, so the ’124 patent does not need to enable the synthesis and development of every conceivable PDE5 inhibitor.

Moreover, Lilly overstates the evidence supporting the amount of work necessary to synthesize, screen, and develop PDE5 inhibitors. For example, Lilly asserts that “[t]he testimony of all the experts (Lilly’s and UroPep’s) demonstrates that screening and synthesizing compounds would, itself, require complicated and lengthy experiments” *Lilly Br.* at 32. Lilly follows this assertion with a long string-cite, thus suggesting that there is ample support for its assertion. But the string-cite does not identify any testimony from any UroPep witness. *Id.* In

fact, as discussed above, Dr. Bell testified that screening and synthesizing PDE5 inhibitors was “routine,” and millions of compounds could be screened in a matter of weeks. Lilly overreaches.

Similarly, Lilly repeatedly asserts that “the number of compounds able to selectively inhibit PDE V is unknowable, but enormous, and very likely within the range of billions.” Lilly Br. at 31. *See also id.* at 4, 9, 15-16, 18-19, 31-34 (discussing the “billions” of compounds). But the bulk of the evidence Lilly identifies – including all the testimony from UroPep’s witnesses – only shows that there may be billions of compounds in the classes of quinazolines or pyrazolopyrimidones; it does not support Lilly’s claim that there may be billions of PDE5 inhibitors. *See, e.g.,* Ex. A, Tr. at 182:9-183:11 (Dr. Ückert testifying that there could be billions of different quinazolines and pyrazolopyrimidones, and that “if any number of these billions of compounds inhibited PDE5 and were used to treat BPH, you would consider that part of your invention”); *id.* at 342:2-23 (Dr. Bell testifying that quinazolines could include billions of compounds, but that the number of PDE5 inhibitors that have been synthesized to date number in the tens of thousands); *id.* at 522:1-17 (Dr. Roehrborn discussing the “tens of thousands of compounds and of chemical structures that would fall within this category”); *id.* at 710:4-16 (Dr. Terrett testifying that one “could conceive of probably billions of compounds” that are “quinazolines and their trimethoxy derivatives,” only “some of which are PDE5 inhibitors”); *id.* at 742:2-7 (Dr. Rotella acknowledging that not all the compounds in the relevant classes would inhibit PDE5). *But see id.* at 749:11-14 (Dr. Rotella discussing the “potentially billions” of selective PDE5 inhibitors, but providing no support for that estimate).

2. The Amount Of Direction Or Guidance Presented

The experts disagreed over the amount of guidance the patent provides. Lilly’s expert, Dr. Roehrborn, testified that, given the number of compounds that could be covered by the claims, the patent should have provided more guidance on how to determine which ones would

work in the invention, including “guidance as to how to study them and how to set up the experiment, [and] how to verify that they actually can be used for the treatment of BPH.”

Id. at 522:1-17. Dr. Bell disagreed:

Q. For instance, does the '124 patent guide a person regarding how to determine whether a clinical candidate or compound is a selective PDE5 inhibitor?

A. Yes. Yes, it tells us how to run IC50 assays and how to confirm those IC50 assays in a tissue strip experiment.

Q. And does the knowledge of a person of skill provide sufficient guidance to determine whether a given selective PDE5 inhibitor can be given in an effective amount to treat BPH?

A. Yes, it does.

Id. at 1296:13-23. Further, Dr. Bell explained that the clinical development of a known PDE5 inhibitor required only “a routine clinical experiment.” *Id.* at 1293:9-18. Lilly’s own witness confirmed that its development of tadalafil for BPH was routine. *Id.* at 949:10-18 (Dr. Viktrup agreeing that his trial testimony addressed “a lot of what happens normally in drug development”). Thus, the evidence at trial showed that the patent provides enough guidance for a person of skill to practice the full scope of claim 1. *See Eli Lilly & Co. v. Actavis Elizabeth LLC*, 435 F. App’x 917, 922 (Fed. Cir. 2011) (“Enablement is not negated if a reasonable amount of experimentation is required to establish dosages and formulation of an active ingredient.” (citing *Enzo Biochem, Inc. v. Calgene Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999)).)

Lilly points to the effort it took Lilly to develop tadalafil, Lilly Br. at 33, and the fact that Dr. Bell’s team at Pfizer “only” identified a “handful of potential clinical PDE V candidates,” *id.* at 36, as evidence of a lack of enablement. But, as Lilly itself has previously noted in a brief to the Federal Circuit, “[e]nablement sufficient to satisfy commercial or FDA standards is not required.” Ex. C, Reply Brief of Plaintiff-Appellant Eli Lilly & Co., *Eli Lilly & Co. v. Actavis*

Elizabeth LLC, No. 2010-1500, 2010 WL 4163191, at *26 (Fed. Cir. Sept. 29, 2010) (citations omitted). Further, Lilly has failed to identify any evidence that Lilly or Pfizer's experiences were unusual, or that the time they took to develop alternative PDE5 inhibitors was due to some deficiency in the '124 patent's disclosure.¹⁰ To the contrary, Dr. Bell testified that this is "how drug discovery works," and agreed with Lilly's attorney that the sorts of obstacles he faced were "pretty common across all pharmaceutical companies." Ex. A Tr. at 1315:3-9; 1316:5-14. Lilly's Dr. Viktrup agreed that Lilly's experience was also normal. *Id.* at 949:10-18. The effort required to develop commercially viable PDE5 inhibitors for BPH does not suggest a lack of enablement. *See Johns Hopkins Univ.*, 152 F.3d at 1360-61 (affirming summary judgment of adequate enablement where patent claimed a genus of antibodies and the specification only described how to make one, where the evidence that others had struggled to synthesize other members of the claimed genus did not demonstrate "a failure of disclosure," noting that "[t]he test for [undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine").

3. The Presence Or Absence Of Working Examples

The '124 patent contains two example formulations for administering sildenafil, a selective PDE5 inhibitor. *See* Dkt, 177-1, '124 patent, col. 6, l. 65 – col. 7, l. 10. One is an injection formulation; the other is a topical formulation. *Id.* *See also* Ex. A, Tr. at 1296:24-1297:10 (Dr. Bell discussing the examples in the patent). Moreover, Dr. Bell testified that a person of ordinary skill would have been familiar with oral formulations for PDE5 inhibitors, which are "one of the most easy formulations to achieve, for most compounds." *Id.* at 1297:7-21.

¹⁰ This argument again represents a misunderstanding of the '124 patent. The patent covers a method of treating BPH. The effort required to develop a PDE5 inhibitor is beside the point.

4. The Nature Of The Invention

Lilly fundamentally misunderstands the nature of the invention. That misunderstanding infects all its invalidity arguments, especially those made under § 112. Lilly repeatedly asserts that, in order to enable the “full scope” of claim 1 of the ’124 patent, UroPep had to enable a skilled person to synthesize and screen billions of compounds. *See, e.g.*, Lilly Br. at 31-32. Not so. As this Court has already found, “the claims of the ’124 patent are directed to the use of PDE V inhibitors to treat BPH, not to the discovery of PDE V inhibitors themselves.” Dkt. 149, Mem. Order & Op. at 30. Dr. Bell’s trial testimony further reinforces that conclusion:

Q. Dr. Bell, I think I just have three questions? Is the ’124 patent about discovering new drugs?

A. That’s an interesting question. It’s a method enabling the discovery of new drugs.

Q. And is the ’124 patent about a treatment method, or is it one of those medicinal chemistry patents like the one we looked at with Dr. Rotella?

A. Yeah. It differs from virtually every other patent that we’ve been discussing over the last few days in that it is only a method of treatment, not a compound patent.

Ex. A, Tr. at 1323:10-21. *See also id.* at 1323:22-1324:8 (Bell noting that “there were a number of clinical candidates already available, ready to go.”). Dr. Bell also confirmed that a person of skill in the art would not “need to discover brand-new PDE5 inhibitors to use the ’124 patent invention.” *Id.* at 1294:25-1295:3.

The patent lists several example PDE5 inhibitors that could be used in the invention, and hundreds of others were available at the time. In this context, enabling a person of ordinary skill to practice the “full scope” of the claim is accomplished by demonstrating that PDE5 inhibitors can work to treat BPH, and describing how to determine whether a given PDE5 inhibitor can be used in the invention. After all, the parties agreed that the person of ordinary skill was:

[A] member of a drug development team with a graduate or post-graduate degree in the following fields: anatomy, pathophysiology, biochemistry, medicinal chemistry, pharmaceutical sciences, or related scientific disciplines, urology and urologic surgery. The drug development team could include analytical chemists, biochemists, clinicians, formulation scientists and other related drug development scientists.

See Dkt. 317-1, Parties' Proposed Jury Instr. at 19-20.

The cases Lilly points to where courts have found a lack of enablement due in part to the number of new compounds that would need to be synthesized relate to patents claiming new compounds, or uses for a truly nascent class of compounds in fields that were “unpredictable” and challenging. See, e.g., *In re Vaeck*, 947 F.2d 488, 495-96 (Fed. Cir. 1991) (affirming lack of enablement of “claims encompassing gene expression in any and all cyanobacteria,” where only “nine genera of cyanobacteria [we]re mentioned in the entire document,” the field was “unpredictable,” and the “claimed genus represent[ed] a diverse and relatively poorly understood group of microorganisms”); *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013) (field was “unpredictable and poorly understood” and “[s]ynthesizing candidate compounds . . . could, itself, require a complicated and lengthy series of experiments in synthetic organic chemistry”). Lilly’s focus on the number of potential PDE5 inhibitors ignores the nature of the invention and the context of what was known to a person of skill in the art at the time. Cf. *Minerals Separation v. Hyde*, 242 U.S. 261, 270-71 (1916) (rejecting validity challenge to claim covering a method for separating metals from other substances, even though “[t]he composition of ores varies infinitely, each one presenting its special problem” where the patent’s disclosure was “sufficiently definite to guide those skilled in the art to its successful application”).

Lilly has not identified a single case where, like here, a patent claimed a new use for a well-known class of compounds in a mature field, and the court required that the specification

enable the synthesis of every possible compound in that class. Such a requirement would have invalidated the patents at issue in *Herschler*, 591 F.2d 693 and *Fuetterer*, 319 F.2d 259.

Moreover, this rule would invalidate numerous existing patents, including many Lilly patents. *See* Dkt. 129, UroPep Opp’n to Lilly SJ Mots. at 35-40 (discussing Lilly’s and others’ patents covering the use of diverse classes of compounds like NSAIDs and CYP2D6 inhibitors).

5. The State Of The Prior Art

As discussed above, *supra* at § IV.C, pp. 12-21, the fields of PDE5 inhibitors, and medications for treatment of BPH, were well developed by July 1997. Lilly’s own expert discussed his extensive utilization of oral medications for treatment of BPH by July 1997. *See* Ex. A, Tr. at 491:20-492:12. And both parties’ experts agreed that over a hundred PDE5 inhibitors, including tadalafil, were known to a person of ordinary skill in 1997. Moreover, by the time of the ’124 patent’s invention, two PDE5 inhibitors – sildenafil and zaprinast – had been subjected to human clinical testing. *Id.* at 318:2-10; 1293:24-1294:3.

Lilly’s motion identifies no evidence that the state of the art was primitive or poorly understood in July 1997. Instead, Lilly wrongly suggests that the Court should ignore the state of the art, arguing that “UroPep’s reliance on the prior art and the knowledge of its own expert . . . cannot be used to substitute for a basic enabling disclosure.” Lilly. Br. at 40-41. But enablement is judged from the perspective of a person of ordinary skill in the art, *see Johns Hopkins Univ.*, 152 F.3d at 1354, and “a patent need not teach, and preferably omits, what is well known in the art, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) (citation omitted). *See also Monsanto Co. v. Scruggs*, 459 F.3d 1328, 1337-38 (Fed. Cir. 2006) (patent covering use of a CaMV promoter did not need to identify any “specific gene sequence” falling within that class of promoters “because of the level of skill in the art and the publicly available

information about CaMV”). The state of the prior art is thus relevant, and enablement must be judged from the perspective of a person of skill in the art at the time.

6. The Relative Skill Of Those In The Art

As detailed above, *supra* at § V.A.4, pp. 31-33, the parties agreed that a person of ordinary skill in the art at the relevant time would be part of a drug development team comprised of highly sophisticated scientists with experience in developing medications. *See* Dkt. 317-1, Parties’ Proposed Jury Instr at 19-20. The Court included that agreed definition in its instructions to the jury. *See* Dkt. 333, Final Jury Instr at 12. The undisputed evidence on this issue weighs in favor of the jury’s enablement finding.

7. The Predictability Or Unpredictability Of The Art

UroPep presented substantial evidence at trial that a person of skill could predict, based on the teachings of the ’124 patent, whether a given PDE5 inhibitor could be used to treat BPH. For example, Dr. Bell testified as follows:

Q. I now want to talk about the question of whether it’s predictable. Once you know PDE5 is in the prostate and functional role, once you have the teachings of the ’124 patent, is it then predictable that a potent PDE5 inhibitor can be given in an effective amount?

A. Yes, I think it is.

Ex. A, Tr. at 1297:22-1298:2. The jury also heard evidence that every potent PDE5 inhibitor could be used in the invention. *Id.* at 334:12-15. Dr. Bell further testified that his team at Pfizer synthesized sildenafil based on existing PDE5 inhibitors, and that people of skill in the art would expect that such new PDE5 inhibitors would have selectivity profiles similar to the other earlier inhibitors on which they were based. *Id.* at 1270:17-1272:8. That evidence alone supports the jury’s finding on enablement.

Faced with this clear evidentiary basis for the jury's findings, Lilly wrongly states that "Dr. Bell himself found that identification of selective, sufficiently potent PDEV inhibitors to treat any disease, including BPH, is *unpredictable*." Lilly Br. at 39 (emphasis in original). To support this claim, Lilly cites, but does not quote, the following testimony:

Q. And that kind of risk and that kind of unpredictability and that kind of lack of success rate is pretty common across all pharmaceutical companies, isn't it?

A. It seems to be, unfortunately.

Ex. A, Tr. at 1316:10-14. Lilly would have the Court believe that the "kind of unpredictability" that Dr. Bell was discussing is the "identification of selective, sufficiently potent PDEV inhibitors." Not so. The immediately preceding testimony shows that the unpredictability Dr. Bell referred to relates to the vicissitudes of the pharmaceutical industry, where companies will sometimes halt development of "beautiful candidates" synthesized by its chemists:

Q. So, you spent six years to identify four candidates, you put three of those into clinical studies, and none of them worked?

A. I didn't say none of them worked.

Q. None of them are approved today?

A. None of them are approved today, but Pfizer made some -- Pfizer and companies made strategic decisions which are completely beyond the control of the chemists who work at the bench to make some beautiful candidates.

Id. at 1316:1-9. Dr. Bell's testimony about "that kind of unpredictability" – the routine facts of life in the pharmaceutical industry – does not support Lilly's position. It just provides more evidence of Lilly's "good for me but not for thee" theory of patent law, where the only applicants that can get patents are pharmaceutical companies who provide no data but get method claims, like Dr. Rotella did for Bristol Meyers Squibb and Lilly did for itself. *See id.* at 839:20-840:21;

845:24-847:6; 849:2-851:7; and 857:13-20 (Dr. Rotella discussing the lack of data in his patent for Bristol Meyers Squibb); Dkt. 129, UroPep Opp'n to Lilly SJ Mots. at 35-40 (discussing Lilly's and others' method claims).

8. The Breadth Of The Claims

As Lilly has acknowledged, claim 1 of the '124 patent is narrower than the full scope of the patent's disclosure. *See* Lilly Br. at 12-15 (arguing that the '124 patent does not support the "narrowed invention of Claim 1"). The '124 patent discusses inhibitors of PDEs 1, 4, or 5, and discusses treatment of numerous prostatic diseases. *See* Dkt. 177-1, '124 patent, col. 2, ll. 17-27; col. 4, ll. 65-68; and col. 7, ll. 35-38. However, claim 1 is limited to the use of an inhibitor of a single PDE, PDE5, for the treatment of a single disease, BPH. *See* Ex. A, Tr. at 1295:15-19. Moreover, Lilly focuses extensively on the number of potential compounds that could be PDE5 inhibitors, but ignores that the patented claim could have been practiced at the time without the discovery or synthesis of a single new compound. *Id.* at 1294:25-1295:3.

Lilly argues that the claims are overly broad because they could potentially cover billions of compounds. But the undisputed evidence showed that there were hundreds of PDE5 inhibitors known in July 1997, and only tens of thousands have been synthesized since. *See id.* at 342:21-24 (Dr. Bell discussing the tens of thousands of PDE5 inhibitors); *id.* at 522:1-17 (Dr. Roehrborn discussing the "tens of thousands of compounds and of chemical structures that would fall within this category"); *id.* at 1254:21-25 ("There were hundreds of selective inhibitors known by July, 1997."). *See also supra* at § V.A.1, pp. 26-28. In a mature field, with hundreds of PDE5 inhibitors known at the time of the invention and high-throughput screening methods available to test thousands more in a matter of weeks, a claim covering the use of a class of compounds to treat a single disease is not overly broad, even if that class contains thousands of species.

B. *Wyeth* Does Not Control This Case

Rather than addressing the *Wands* factors, Lilly bases its enablement motion almost entirely on *Wyeth & Cordis Corp.*, 720 F.3d at 1380, describing that case as “especially instructive,” Lilly Br. at 28, and as “controlling in this strikingly similar fact pattern,” *id.* at 30. Lilly’s reliance on *Wyeth* is misplaced. As an initial matter, Lilly omits critical parts of the *Wyeth* decision. For example, Lilly’s first significant quote from *Wyeth* states that “[c]laims are not enabled when, at the effective filing date of the patent, one of ordinary skill in the art could not practice *their full scope*.” Lilly Br. at 27 (quoting *Wyeth*, 720 F.3d at 1384). But the sentence does not end there. The sentence in *Wyeth* continues, and adds the following caveat: “without undue experimentation.” *Id.* Lilly thus omits the key enablement standard – undue experimentation (which *Wyeth* later refers to as “[t]he central issue on appeal”), *id.* at 1384 – suggesting that there is a separate full scope requirement that, if not met, will invalidate the ’124 patent.¹¹ Of course that is not true.

Moreover, there are significant factual differences between this case and *Wyeth*. The *Wyeth* patents related to “the use of rapamycin for the treatment and prevention of restenosis, which is the renarrowing of an artery.” *Id.* at 1381. The court construed “rapamycin” to cover sirolimus, and “any structural analog of sirolimus that exhibits immunosuppressive and antirestenotic effects.” *Id.* at 1384. However, the patents only disclosed sirolimus; they did not disclose any analogues. *Id.* at 1383. The patent’s lack of disclosure of any analogues was a central factor in both the district and appellate courts’ conclusions in *Wyeth*. *Id.* at 1384; *Wyeth v. Abbott Labs.*, Civ. No. 08-230 (JAP), 2012 WL 175023, at *17 (D.N.J. Jan. 19, 2012). In this case, the patent disclosed several example selective PDE5 inhibitors that could have been used in

¹¹ *Wyeth* also does not italicize “their full scope,” an alteration that Lilly did not acknowledge.

the invention at the time. *See* Dkt. 177-1, '124 patent at col. 2, l. 28 – col. 4, l. 44; Ex. A, Tr. at 514:24-515:4; 1259:1-21; 1260:24-1261:9; Dkt. 190-6, Takase 1993, at 2.

Second, unlike the hundreds of selective PDE5 inhibitors that were known in July 1997, Ex. A, Tr. at 1254:21-25, there were only four potential sirolimus analogues known in the art at the time of the invention in *Wyeth*. And there was no evidence that a person of skill would have known whether those analogues had the claimed effects at the time of the invention. *See Wyeth & Cordis Corp.*, 720 F.3d at 1385 (noting that Wyeth asserted the known analogues had those effects based “in part on expert testing performed in the course of the litigation;” such testing would not have been necessary if those effects were well-known at the time of the invention). The claims in *Wyeth* covered a potentially large class of sirolimus analogues with certain immunosuppressive and antirestenotic effects, but the patents did not disclose a single such analogue and a person of ordinary skill in the art would not have been aware of one. The inventors in *Wyeth* thus did not set forth a single mode of practicing the invention with an analogue of sirolimus, which “is equivalent to non-enablement.” *See In re Glass*, 492 F.2d 1228, 1233 (C.C.P.A. 1974). There is no dispute that the '124 patent disclosed and enabled multiple modes of practicing its invention, so the unique problems presented by *Wyeth* simply do not apply to this case.

Third, the evidence in *Wyeth* showed that “[s]ynthesizing candidate compounds . . . could, itself, require a complicated and lengthy series of experiments in synthetic organic chemistry.” *Wyeth & Cordis Corp.*, 720 F.3d at 1386. The underlying district court decision provides additional context for the Federal Circuit’s findings. There, the court noted as follows:

[T]here are several chemical and physical properties that contribute to the challenge of formulating rapamycin and administering rapamycin for a particular indication. The record shows that rapamycin is a large molecule that is substantially insoluble in

water and poorly soluble in oils. It has a melting point over 180 degrees, thus it is a solid at room temperature and body temperature. It is lipophilic, which can make it difficult to release from a carrier into human tissue. It is chemically reactive and subject to rapid degradation and decomposition.

Wyeth, 2012 WL 175023, at *11. Further, the patentee in *Wyeth* had admitted “that it found rapamycin to be a ‘major challenge’ and ‘extraordinarily difficult to formulate.’” *Id.* In contrast, there is no evidence that synthesizing PDE5 inhibitors posed any significant challenges.

Fourth, the field at issue in *Wyeth & Cordis Corp.* was “unpredictable and poorly understood.” 720 F.3d at 1386. As the district court explained, “the inventors recognized that then-existing knowledge regarding rapamycin and its mechanism of action was in a very early stage.” *Wyeth*, 2012 WL 175023, at *15. As discussed above, *supra* at § IV.C, pp. 12-21, the field of the art addressed by the ’124 patent was well-established. *Cf. Abbott Biotechnology Ltd. v. Centocor Ortho Biotech, Inc.*, 35 F. Supp. 3d 163, 179 (D. Mass. 2014) (“Centocor’s analogy to *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013), is not dispositive. . . . While similarities to the present case are apparent, certain facts that could distinguish the cases—such as predictability, how routine and burdensome testing was, and the utility of the guidance and direction offered by the patents—remain unknown, rendering summary judgment inappropriate.”).

C. The ’124 Patent Enables A Person Of Skill In The Art To Determine Whether A PDE5 Inhibitor Is Selective Enough To Be Used In The Invention

Lilly also argues that claim 1 of the ’124 patent is not enabled because the patent did not adequately disclose how to determine whether a given PDE5 inhibitor met the claimed selectivity requirement. *See Lilly Br.* at 37-39. As an initial matter, Lilly waived the right to raise

this issue on a motion for JMOL because Lilly did not raise it during its Rule 50(a) motion.¹² In addition, UroPep presented substantial evidence that the '124 patent enabled a person of skill in the art to determine whether a given compound met the patent's selectivity requirement. Lilly points to the testimony of its expert, Dr. Beavo, to support its argument that claim 1 of the '124 patent did not enable a person of skill to determine the selectivity of a given PDE5 inhibitor. But we must assume that the jury credited Dr. Bell's contrary testimony:

Q. Do you agree with Professor Beavo that the methods in the '124 patent could not be used to identify PDE5 selective inhibitors?

A. No, I don't. The methods they use to measure potency and selectivity are very common and are commonly used throughout the industry.

Q. And when you say that, what methods were used at Pfizer for sildenafil or Viagra?

A. So, essentially the same methods as set down here, Galwan and Nicholson.

Ex. A, Tr. at 1284:7-16. *See also id.* at 1267:13-21 (the methods for testing selectivity described in the '124 patent are "very similar" to the methods "used by the Eisai company" and by Pfizer).

Dr. Bell further testified that the disclosure in the patent would have enabled a person of ordinary skill in the art to practice the claims:

Q. Given the knowledge of a person of skill in 1997, did the patent present sufficient direction or guidance to practice the claims?

A. Yes, I think it does.

¹² Lilly's Rule 50(a) motion on enablement was limited to challenging the breadth of claim 1, not its selectivity requirement. Ex. A, Tr. at 1392:15-18 ("Third, the enablement issue, that the evidence in the record proves by clear and convincing evidentiary standard that the claims are not enabled to their full scope."). Because Lilly did not raise a challenge to enablement of the selectivity requirement during trial, it cannot raise it as part of a Rule 50(b) motion.

Q. For instance, does the '124 patent guide a person regarding how to determine whether a clinical candidate or compound is a selective PDE5 inhibitor?

A. Yes. Yes, it tells us how to run IC50 assays and how to confirm those IC50 assays in a tissue strip experiment.

Q. And does the knowledge of a person of skill provide sufficient guidance to determine whether a given selective PDE5 inhibitor can be given in an effective amount to treat BPH?

A. Yes, it does.

Id. at 1296:9-23. Substantial evidence supports the jury's conclusion that a person of skill could apply the patent's teachings to determine whether a PDE5 inhibitor was sufficiently selective.

VI. INDEFINITENESS

This Court has already rejected Lilly's indefiniteness arguments as a matter of law. *See* Dkt. 234, Mem. Op. & Order at 28-47. *See also* Dkt. 294, Order re UroPep Mot. to Preclude at 5-6 ("[T]he issue of indefiniteness has been resolved. The Court's March 3, 2017, order held that the claim language, as construed by the Court, is 'sufficiently definite to satisfy the requirements of section 112, paragraph 2, of the Patent Act,' and that 'the claims of the '124 patent are not invalid for indefiniteness.'"). For all the reasons identified in the Court's ruling, UroPep's briefs, *see, e.g.*, Dkt. 189, UroPep Opp'n to Lilly SJ Mot.; Dkt. 217, UroPep Sur-Reply in Opp'n to Lilly SJ Mot.; Dkt. 238, UroPep Opp'n to Lilly Mot. to Suppl., and the supporting evidence UroPep submitted with its briefs, JMOL of indefiniteness is not warranted.

Despite finding that claim 1 of the '124 patent was not indefinite as a matter of law, the Court denied UroPep's motion to preclude Lilly from presenting evidence at trial that was relevant to the issue of indefiniteness. *See* Dkt. 294, Order re Mot. to Preclude at 11. The Court did not permit Lilly to introduce evidence contradicting the Court's claim construction, *id.*, but the Court allowed Lilly to introduce evidence relating to the issue of indefiniteness, *id.* at 9-11.

Lilly chose not to take advantage of that opportunity. At trial, Lilly never responded to Dr. Bell's declarations explaining that a person of skill in the art would have readily understood the selectivity requirement to require a comparison of IC₅₀ ratios, and that such a comparison could be reliably accomplished under the right conditions. *See* Dkt. 189-1, Bell Decl. ¶¶ 14-16, 26-34, 36-43, 57-61, 76, 79-86, and 105; Dkt. 238-2, Bell Decl. ¶¶ 1-17.

Dr. Bell's trial testimony further supports the Court's finding that the claims are not indefinite. As discussed above, Dr. Bell testified at trial that Galwan and Nicholson – two of the three articles referenced in the '124 patent – described methods “to measure potency and selectivity [that] are very common and are commonly used throughout the industry.” Ex. A, Tr. at 1284:7-16. Dr. Bell also addressed the Truss article at trial, explaining that it was “signposting” a “fractionation method similar to the one that had been applied to the pig bladder.” *Id.* at 1284:17-1285:7. Further, on cross-examination, Lilly's expert Dr. Beavo conceded that Truss described a “peak fractionation” method, *id.* at 695:6-22, that was similar to the method that Pfizer used to determine the selectivity of sildenafil, *id.* at 702:5-703:4. The trial record presents no reason for the Court to revisit its rejection of Lilly's indefiniteness defense.

VII. OBVIOUSNESS

When a claimed invention would have been obvious to a person having ordinary skill in the art at the time of the invention, the patent is invalid. 35 U.S.C. § 103. A party seeking to invalidate a patent as obvious must show “by clear and convincing evidence that a skilled artisan would have had reason to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so.” *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1068-69 (Fed. Cir. 2012).

Though obviousness is a question of law based on underlying factual findings, *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966), it may be submitted to the jury with a proper instruction. *In re Hayes Microcomputer Prod., Inc. Pat. Litig.*, 982 F.2d 1527, 1539 (Fed. Cir. 1992). “When the jury is supplied with sufficient valid factual information to support the verdict it reaches, that is the end of the matter. In such an instance, the jury’s factual conclusion may not be set aside by a JMOL order.” *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1355 (Fed. Cir. 2001) (reversing district court’s JMOL of obviousness).

A. The Jury Heard Sufficient Factual Information To Support Its Verdict That The ’124 Patent Is Not Invalid For Obviousness

The ’124 patent claims the use of a PDE5 inhibitor to treat BPH. At trial, Dr. Ückert testified that the inventors discovered PDE5 in the prostate. Ex. A, Tr. at 161:14-163:23. Dr. Ückert also testified that the inventors conducted tissue bath experiments using PDE5 inhibitors on human tissue to determine the functional relevance of PDE5 in the prostate. *Id.* at 166:14-25. As a result of these tests, the inventors discovered that PDE5 inhibition relaxes smooth muscle tissue in the prostate. *Id.* at 168:9-17. From these novel ideas, the inventors concluded that PDE5 inhibitors could be used to treat BPH. *Id.* at 170:13-24. This evidence alone suffices to support the jury’s verdict of non-obviousness. And Lilly identified no evidence at trial contradicting Dr. Ückert’s account of the inventors’ discovery of the presence and functional role of PDE5 in the prostate.

Further, Dr. Bell testified that it is impossible to predict which PDE would be present in what organ. *Id.* at 1285:12-17. And knowing that a PDE is present in an organ tells you nothing about the importance of the PDE in that organ. *Id.* at 1285:18-25. For example, PDE5 is present in the prostate, bladder, and lungs, but PDE5 only has a functional role in the prostate; it plays no functional role in the bladder or the lungs. *Id.* at 1286:16-1288:11.

The jury also heard testimony about, and was instructed on, objective considerations of non-obviousness such as commercial success. UroPep's damages expert Dr. Vellturo explained that Lilly's ability to promote the treatment of BPH using a PDE5 inhibitor provided significant commercial success for Lilly (leading to more than \$700 million in infringing sales), allowing it to reach its all-time goal of overtaking Viagra in sales. *Id.* at 375:1-18.

Nothing Lilly offered at trial and nothing Lilly states in its JMOL motion could warrant overturning the verdict.¹³ Lilly's motion largely recites facts known in the art at the time of the invention and stated in the patent. Lilly Br. at 43-44 (e.g., that BPH is a growth of the prostate and may result in urination difficulties, that relaxing smooth muscle cells can help alleviate urination difficulties, that increasing cAMP and cGMP levels in smooth muscle cells can relax the smooth muscle, and that PDE inhibitors can relax smooth muscle cells by reducing the digestion of cAMP and cGMP). The jury knew the patent office was aware of these facts when issuing the '124 patent and nevertheless found the patent non-obvious. Ex. A, Tr. at 1444:6-15.

Lilly also relies on an article by Dr. Burnett, a PDE expert, to say it was known as early as 1994 that the NO-cGMP pathway is functional in the prostate. Lilly Br. at 45. But this was controverted by the evidence at trial. Lilly's own expert admitted Burnett's article is silent about whether PDE5 (1) was in the prostate, or (2) played a functional role in the prostate. Ex. A, Tr. at 598:3-22. In fact, none of the articles reviewed by Lilly's expert said that PDE5 was found in the prostate or played a functional role in the prostate. *Id.* at 600:8-18. Further, UroPep's expert explained that while the Burnett article talks about cGMP and the NO-cGMP pathway, it does

¹³ Lilly purports to incorporate its pre-verdict JMOL motion on obviousness. Lilly Br. at 43. But the entirety of that motion is "that the evidence in the record proves by [the] clear and convincing evidentiary standard that the claims are obvious in view of the evidence." Ex. A, Tr. at 1392:19-22. The motion was denied. *Id.* at 1392:23-24.

not point toward PDE5. *Id.* at 1290:6-1292:7. In fact, Dr. Bell testified that the Burnett article taught away from the presence and functional role of PDE5 in the prostate and pointed, instead, “towards PDE3 inhibition as being important in the prostate.” *Id.* at 1291:11-1292:1.

Rather than acknowledging its own expert’s admissions, Lilly argues (for the first time) that UroPep’s 1997 patent application described the use of PDE1, PDE4, and PDE5 to treat a variety of prostatic issues, and not the use of only PDE5 to treat only BPH. Lilly Br. at 45. The implication is that UroPep’s reference to PDEs other than PDE5 being in the prostate is akin to Burnett’s inability as of the mid-1990s to identify any PDEs in the prostate. It is not clear how this statement supports Lilly’s obviousness argument. As Dr. Ückert testified, UroPep found PDE5 in the prostate. Ex. A, Tr. at 163:18-23. Burnett did not. *Id.* at 600:8-18.¹⁴

Lilly’s argument, essentially that the jury got it wrong, is based on the same hindsight bias the jury heard about at trial. *Id.* at 615:8-618:21. Given Dr. Ückert’s testimony, Lilly’s expert’s admissions, and the jury’s awareness of what the patent office knew before issuing the ’124 patent, ample evidence supports the jury’s finding. There is no reason to reject it on JMOL.

VIII. ANTICIPATION

A. The Legal Standard

A prior art reference anticipates a claimed invention only when it discloses every feature of the claimed invention. *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1375

¹⁴ Lilly also argues that it was obvious to treat BPH with a PDE5 inhibitor because a PDE5 inhibitor had been used to treat erectile dysfunction. Lilly Br. at 46-47. Similarly, Lilly states that “to the extent that the alleged invention of claim 1 is based on the recognition that the PDE inhibition required for relaxation of prostrate [sic] muscle was different from the PDE inhibition required for treating impotence, that distinction is also not recognized or discussed in the ’124 patent.” Lilly Br. at 46. These arguments are unavailing, for the jury weighed UroPep’s evidence (that the invention of claim 1 is based on the inventors’ discovery that PDE5 was in the prostate and that PDE5 had a functional role in the prostate) against Lilly’s evidence that PDE5 was used to treat penile tissue, and yet decided that UroPep’s invention was not obvious.

(Fed. Cir. 2006). Inherent anticipation can be found “only when the reference discloses prior art that must *necessarily* include the unstated limitation.” *Transclean Corp. v. Bridgewood Servs., Inc.*, 290 F.3d 1364, 1373 (Fed. Cir. 2002) (internal citation omitted). Inherency “may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.” *U.S. Water Servs., Inc. v. Novozymes A/S*, 843 F.3d 1345, 1350 (Fed. Cir. 2016) (internal citation omitted).

Anticipation is a question of fact, including whether or not an element is inherent in the prior art. *Eli Lilly & Co.*, 471 F.3d at 1375. That is why “[a] district court may overturn a jury’s verdict on a motion for JMOL only if, upon the record before the jury, reasonable persons could not reach the verdict returned by that jury.” *Union Oil Co.*, 208 F.3d at 994 (affirming denial of JMOL that patent was anticipated). Despite the factual nature of the anticipation inquiry, Lilly again asks the Court to invalidate the ’124 patent.¹⁵ The request should again be denied.

B. Printed Publication

An anticipatory reference meets the printed publication requirement when a person of skill in the art “exercising reasonable diligence, can locate it.” *Blue Calypso, LLC v. Groupon, Inc.*, 815 F.3d 1331, 1348 (Fed. Cir. 2016). It is Lilly’s burden to show by clear and convincing evidence that Cheung, its lone anticipatory reference, meets this requirement. Dkt. 234, Mem. Op. & Order at 24. Lilly provided no credible evidence that Cheung is a printed publication.

First, Lilly offered no evidence that Cheung was catalogued in any library by July 1997. The only witness who could have testified to that fact was Mr. LaForgia. But even if we accept

¹⁵ Lilly’s motion marks the fourth time it has asked the Court to find the ’124 patent anticipated as a matter of law. The first three attempts were unsuccessful. *See* (1) Dkt. 172, Lilly Mot. for Summary Judgment of Anticipation, rejected at Dkt. 234, Mem. Op. & Order at 20-28; (2) Ex. A, Tr. at 464:23-465:1, Lilly Rule 50 catch-all motion, rejected at *id.* at 472:15-17; and (3) *id.* at 1392:3-9, Lilly Renewed Rule 50 motion on anticipation, rejected at *id.* at 1392:23-24.

his testimony that Cheung was in the American College of Traditional Chinese Medicine (“ACTCM”) library on that date, there is no evidence it was catalogued at all, let alone in a way that would help a person of skill in the art locate the reference. Rather, Mr. LaForgia testified he did not know how books were catalogued at ACTCM. Ex. A, Tr. at 901:9-12.¹⁶

Lilly instead contends that Cheung was publicly available to a person of skill because the Harmonious Sunshine Cultural Center sent brochures to a mailing list. Lilly Br. at 47. But there is no evidence that a person of skill was on the mailing list. Mr. LaForgia never worked at the Sunshine Center, Ex. A, Tr. at 902:3-6, never played a role in maintaining the brochures, *id.* at 902:14-16, and never looked over the mailing list with Cheung, *id.* at 902:24-903:1. Mr. LaForgia only testified that he and a fellow acupuncturist received the brochure. *Id.* at 903:4-21. But they are not persons of skill in the art. *See* Dkt. 333, Jury Instr at 12. That they could locate Cheung is not evidence that Cheung was publicly available to a person of skill.

C. Cheung Does Not Disclose Each And Every Element Of The ’124 Patent

Claim 1 of the ’124 patent requires that a PDE5 inhibitor be administered in an “effective amount.” Dkt. 177-1, ’124 Patent. Because Cheung does not necessarily disclose or include the “effective amount” limitation, it fails to anticipate the ’124 patent on the merits as well. *Transclean Corp.*, 290 F.3d at 1373 (inherent anticipation requires “the reference discloses prior art that must *necessarily* include the unstated limitation”).

First, Cheung discloses administering a “basic formula” to its subjects. Dkt. 187-1, Trial Ex. 1551, at 80-81. The basic formula contains several ingredients other than Horny Goat Weed. *Id.* Even assuming that the basic formula treated BPH, there is no way to tell whether the

¹⁶ Further, Mr. LaForgia never attended ACTCM, Ex. A, Tr. at 900:14-16, never worked at the ACTCM library, *id.* 900:12-13, and was not a librarian, *id.* at 900:4-5.

patients' improvements resulted from the Horny Goat Weed or one of the several other ingredients.¹⁷ When asked at trial whether he knew if it was icariin that was responsible for the reported effects, Lilly's expert admitted "[i]t is possible that there are some compounds in the other herbs having an effect on the prostate or the symptoms." Ex. A, Tr. at 573:6-16. That possibility alone is sufficient to deny Lilly's motion. *U.S. Water*, 843 F.3d at 1350 (inherency "may not be established by probabilities or possibilities").

Second, Cheung's basic formula is comprised of one set of ingredients "or" another set of ingredients, and Cheung does not disclose which set was actually administered in the "study." *See* Dkt. 187-1 at 80-81. Only one set includes Horny Goat Weed, which means Cheung does not necessarily disclose a single person being given a formula containing Horny Goat Weed to treat BPH.¹⁸ Cheung cannot inherently anticipate the patent based on a formula that may not contain Horny Goat Weed.¹⁹

Third, Cheung characterizes several symptoms as being associated with BPH that are not in fact associated with BPH. Dkt. 187-1 at 80 (noting that Cheung's BPH "study" addressed the following symptoms: fatigue, shortness of breath, backache, dull purplish red tongue thin white

¹⁷ This Court recognized this problem in its Order denying Lilly's motion for summary judgment on anticipation. Dkt. 234, Mem. Op. & Order at 26 ("[T]he herbal remedies given to Dr. Cheung's patients included many ingredients other than Horny Goat Weed, which calls into question whether it was the Horny Goat Weed, rather than some other ingredient in the formulation given to the patients, that was responsible for the favorable reported results.").

¹⁸ This Court also recognized this issue, noting that "the clinical results for the 34 patients were reported with regard to a formulation in which Horny Goat Weed was not a necessary component, but only an optional one." Dkt. 234, Mem. Op. & Order.

¹⁹ Lilly does not contest that the "or" in Cheung means it is possible that no subject received a formula containing Horny Goat Weed. Instead, Lilly says anticipation only requires an "enabling disclosure" and that "actual administration . . . is irrelevant." Lilly Br. at 50-51. But Lilly cannot base the "effective amount" limitation on Cheung's results while also admitting that the administered formula may not even contain Horny Goat Weed.

or exfoliating fur or cracks, sublingual venous dilatation, and increase of capillary beds).²⁰ As Lilly highlights in its motion, Lilly Br. at 49-50, Cheung reported a total effective rate of 94.12%. Dkt. 187-1 at 81. But because the study considered symptoms unrelated to BPH, Cheung does not necessarily disclose an improvement in BPH symptoms; the improvements could have been in unrelated symptoms (e.g., fatigue, or dull purplish red tongue). With no disclosure in Cheung that Horny Goat Weed was used to treat BPH, it cannot anticipate the '124 patent.

Fourth, there was unrebutted testimony at trial that the amount of icariin in Horny Goat Weed was below .05%, and that a patient would need to consume approximately 3.5 pounds of Horny Goat Weed per day to achieve the same PDE5 inhibiting effect as a 5 mg dose of tadalafil. Ex. A, Tr. at 1248:2-1249:18. No Lilly expert disputed this calculation.²¹ Yet the basic formula disclosed in Cheung contained (at best) just 15 grams of Horny Goat Weed. There is thus evidence that the amount of Horny Goat Weed in Cheung (if any) was just a tiny fraction of the amount needed to treat BPH. Lilly notes there is no dosage requirement in the '124 patent and argues that Cheung discloses an effective amount because of the 94% effective rate. Lilly Br. at 50.²² But for the reasons noted above, the effective rate Cheung reports does not support the

²⁰ Again, this Court has recognized this problem before. Dkt. 234, Mem. Op. & Order at 25-26.

²¹ Lilly points to testimony from Dr. Bell, saying that it “established that the amount of icariin disclosed in Cheung is remarkably similar to the amount of zaprinast.” Lilly Br. at 50 (citing Ex. A, Tr. at 1321:3-1323:1). But that is not what Dr. Bell said. Rather, Dr. Bell testified that he compared the potency of icariin to tadalafil, not zaprinast. Ex. A, Tr. at 1321:3-1323:1. There was no testimony about a comparison between icariin and zaprinast. Lilly also cites Dkt. 177-27, Trial Ex. 1328, Ning 2006, though that article states that “icariin was generally three times less potent than zaprinast in suppressing the cGMP-hydrolytic activity of PDE5 isoforms.” Dkt. 177-27 at 1353.

²² Lilly also says UroPep is attacking whether using Cheung’s basic formula has commercial utility. Lilly Br. at 49-50. It is true that Cheung’s formula is unlikely to be a commercially viable product. But that is not UroPep’s main argument. Rather, UroPep’s argument is that because

effectiveness of 15 grams of Horny Goat Weed because (1) it is unclear what ingredients are in the formula, (2) it is unclear what ingredients are potentially alleviating the symptoms, and (3) it is unclear whether the alleviated symptoms are associated with BPH.

Fifth, Lilly's expert conceded that the American Urological Association's consensus opinion is that Horny Goat Weed is not a recommended treatment of LUTS secondary to BPH. Ex. A, Tr. at 565:20-566:3. Lilly responds that it is uncontroverted that the '124 patent does not exclude phytotherapy. Lilly Br. at 51. But that is beside the point. The question is whether Cheung discloses an effective amount of a selective PDE V inhibitor to treat BPH. On this point, Lilly's expert's admission suggests that any amount of Horny Goat Weed may not effectively treat BPH, let alone the small levels potentially included in one of Cheung's formulations.

Other errors abound in Lilly's motion. Lilly states that an anticipatory reference need only enable and describe the claimed invention. Lilly Br. at 49 (citing *Arthrocare Corp. v. Smith & Nephew, Inc.*, 406 F.3d 1365, 1371-72 (Fed. Cir. 2005) (quoting *In re Paulsen*, 30 F.3d 1475, 1479 (Fed. Cir. 1994))); *see also id.* at 50 ("anticipation 'requires only an enabling disclosure'") (quoting *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373 (Fed. Cir. 2003)). The suggestion is that prior art that does not disclose each limitation in the claimed invention can nonetheless anticipate a patent so long as it enables the claimed invention.

But that is not the law. As noted in both *Arthrocare* and *Paulsen*, anticipatory prior art must disclose each limitation *and* enable a person of skill in the art to possess the invention. *See In re Paulsen*, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994) (Anticipation "requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. In addition,

there was only 15 grams of Horny Goat Weed (at most) in the basic formula, a juror had reason to decide that the amount of icariin in the formulation was not an effective amount.

the reference must be enabling” (internal citation omitted)). And Lilly’s reliance on *Schering* only highlights its error. In *Schering*, the court held that a prior art reference that did not expressly disclose any limitation could nonetheless inherently anticipate. *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373, 1378-81 (Fed. Cir. 2003). But there was no dispute in *Schering* that the prior art reference necessarily disclosed each limitation of the claimed invention. *Id.* That is not the case here, where there are several reasons to question whether Cheung inherently discloses key claimed limitations.²³

IX. CLAIM CONSTRUCTIONS PREVIOUSLY PRESENTED BY THE PARTIES SUPPORT NEITHER JMOL NOR A NEW TRIAL

Lilly states that adoption of any previously proposed construction of “inhibitor of phosphodiesterase (PDE) V” warrants JMOL for Lilly. Lilly Br. at 51-52. This is just not true.

First, UroPep explained in response to Lilly’s motion for summary judgment of noninfringement that Lilly infringes the ’124 patent even if “inhibitor of phosphodiesterase (PDE) V” was construed under § 112, ¶ 6. Dkt. 129, UroPep Resp. at 43-46. At a minimum, there is a question of fact precluding JMOL in Lilly’s favor under this alternate construction.

Second, Lilly states that eliminating the selectivity requirement of an “inhibitor of phosphodiesterase (PDE) V” would render the claim invalid for failure to meet the written description or enablement requirement “for the reasons discussed above.” Lilly Br. at 51.²⁴ It is

²³ Lilly raises the “enabling disclosure” argument for the first time in its post-trial Rule 50(b) motion. It has thus been waived. *In re Isbell Records, Inc.*, 774 F.3d 859 (5th Cir. 2014). Regardless, that an anticipatory reference must enable a person of skill to practice the invention (in addition to disclosing each limitation) provides an additional ground to deny Lilly’s motion, for Lilly provided no evidence that Cheung enabled the claimed invention. Cheung’s basic formula contains several plant ingredients and an untold number of compounds in each plant. Even assuming that the Cheung formula treats BPH, a person of skill would have to conduct significant experimentation to identify which compound is driving the results.

²⁴ Lilly falsely asserts that UroPep proposed a construction that did not include a selectivity requirement. Lilly Br. at 51. UroPep said that “a POSITA would further understand that an

not clear what Lilly means, for there is no cite identifying the “reasons discussed above.” Nothing in Lilly’s written description argument could be read to say that eliminating the selectivity requirement generates a written description problem for UroPep. And Lilly’s enablement argument is that the selectivity requirement adds an enablement problem for UroPep. *Id.* at 37-39. If anything, adopting a construction that eliminates the selectivity requirement would eliminate any enablement problem and have no effect on written description.

Third, Lilly says that construing “inhibitor of phosphodiesterase (PDE) V” to require selectivity as compared to PDEs 1-7 would entitle it to JMOL for failure to meet the written description and enablement requirements. Lilly again points, without citation, to the “reasons discussed above,” despite the fact that nothing in Lilly’s written description or enablement sections addresses the impact this new construction would have on its arguments. *Id.* at 51. Lilly also states that UroPep conceded that none of the disclosed compounds are 20-fold selective for PDE V versus PDE VI. *Id.* at 51-52 (citing Motions Hearing, Feb. 27 [*sic*], 2017 Tr. at 19:3-12). That is not what UroPep said. UroPep said that if none of the examples in the patent were selective for PDE VI at the 20 times margin, then the patent could be invalid for written description. Ex. D, Feb. 21, 2017 Hearing Tr. at 18:21-25. However, UroPep then stated that to the extent it is unclear whether certain compounds were selective for five over six, the

inhibitor of PDE V infers a requirement that the inhibitors are both potent and relatively selective for PDE V.” Dkt. 109, Claim Constr. Reply Br. at 10. The Court recognized UroPep’s advocacy for a selectivity requirement. *See* Dkt. 149, Order at 6-7 (“In addition, UroPep asserts that the intrinsic record requires that the phrase should be understood to contain three additional limitations: the PDE V inhibitor must be ‘selective’ . . .”). This is not the first time Lilly has made this incorrect assertion, *see* Dkt. 193-1, Lilly Opp’n to MSJ on Infringe at 9 n.1 (representing that UroPep offered a claim construction “without any selectivity requirement at all”), and is not the first time it has been informed of its mistake, Ex. D, Feb. 21, 2017 Hearing Tr. at 36:10-37:1.

uncertainty inures to UroPep's benefit, as Lilly bears the burden of proving invalidity. *Id.* at 18:25-19:10.

Fourth, Lilly says that if "inhibitor of phosphodiesterase (PDE) V" is construed to require selectivity as compared to all PDEs 1-11, then Lilly is entitled to JMOL on infringement because tadalafil is not selective as to PDE11A1. Lilly Br. at 52. But as UroPep previously noted, PDE11A1 is not found in the prostate. Dkt. 189, UroPep Resp. to Lilly MSJ at 27. The only PDE11 in the prostate is PDE11A4. *Id.* And Tadalafil is more than 20 times more selective for PDE5 than for PDE11A4. Dkt. 158-2, Cialis label at Section 12.1.

Finally, Lilly states in a single sentence that it is entitled to a new trial because the Court's claim constructions were erroneous. Lilly Br. at 52. But an erroneous claim construction alone is insufficient for a new trial; the erroneous claim construction must have prejudiced Lilly. *Eaton Corp. v. Rockwell Int'l Corp.*, 323 F.3d 1332, 1344 (Fed. Cir. 2003) (holding that new claim construction does not, in and of itself, require a new trial; the moving party must show that the error was prejudicial). Lilly has identified no prejudice.

X. THE GROUNDS FOR LILLY'S MOTIONS FOR JUDGMENT AS A MATTER OF LAW DO NOT SUPPORT A NEW TRIAL

Lilly says in a single sentence – offering no analysis and citing no case – that "each of the bases for JMOL" also warrants a new trial. Lilly Br. at 52. In any case, the standards are different. JMOL (Rule 50) requires showing there is no legally sufficient evidentiary basis for the jury's finding, while a new trial (Rule 59) requires showing that a new trial is necessary to "prevent an injustice." *Seibert v. Jackson Cty., Miss.*, 851 F.3d 430, 438 (5th Cir. 2017). Lilly has identified no injustice here.

XI. THE COURT’S JURY INSTRUCTION ON ENABLEMENT WAS NOT ERRONEOUS AND DOES NOT WARRANT A NEW TRIAL

Lilly contends that a new trial is warranted because the Court should have instructed the jury that the ’124 patent must enable both the treatment and prophylaxis of BPH. A new trial may only be granted if doing so is necessary to “prevent an injustice.” *Seibert*, 851 F.3d at 438. But there is no injustice here. As this Court held, Lilly sought an instruction on enablement that was not supported by the facts at trial, would have been confusing to the jury, and was based on a principle that was already incorporated in the jury instructions. Dkt. 359, Mem. Op. at 7-10.

First, the evidence in this case from both parties focused on the treatment of BPH. *Id.* at 7-8. Where prophylaxis was discussed at all, it was in the context of treatment. *Id.* To challenge the Court’s finding that the evidence focused on treatment, Lilly points to two half-pages of transcript. Lilly Br. at 53. But as the Court already acknowledged, this does not show that prophylaxis was a focus at trial. Dkt. 359, Mem. Op. at 8. On the contrary, prophylaxis and treatment were treated together as a single process. *Id.* Put another way, the Court’s enablement instruction did not harm Lilly because there was no evidence at trial for a jury to find, by clear and convincing evidence, that “treatment” was enabled while “prophylaxis” was not.

Second, Lilly disputes this Court’s holding that the terms “prophylaxis” and “treatment” do not describe distinct processes. Lilly Br. at 53. The Court first acknowledged this in its initial claim construction order, noting that “as UroPep’s expert explained, there was ‘no clear distinction [drawn] between prophylaxis and treatment for BPH.’” Dkt. 359, Mem. Op. at 8 (quoting Dkt. 131, Claim Constr. Order at 9). That is largely because of the overlapping nature of the two terms. *Id.* at 8-9. For that reason, “a course of medication designed to deal with the condition could be regarded as either prophylaxis or treatment” of BPH. Dkt. 131, Claim Constr. Order at 9. As this Court notes, Lilly made no attempt at trial to show that a different analysis

was required for enabling a “prophylaxis” limitation as opposed to a “treatment” limitation. Dkt. 359, Mem. Op. at 9.²⁵

In its brief Lilly asserts, without citation and for the first time, that “‘prophylaxis’ can occur without an enlarged prostate or any lower urinary tract symptoms.” Lilly Br. at 53. That statement is dubious, given that Lilly has repeatedly represented to this Court that “to directly infringe the claimed method of treatment or prophylaxis of ‘benign prostatic hyperplasia,’ an enlarged prostate must be present in the patient who is administered Cialis.” Dkt. 193-1, Lilly Corrected Opp’n to MSJ at 14.²⁶

Third, the Court instructed the jury that the specification must enable the full scope of the claim, not just a single embodiment. Dkt. 359, Mem. Op. at 9. *See also* Ex. A, Tr. at 1427:25-1428:13 (enablement instruction). Lilly contends that the jury may not have understood what it means to fully enable a claim. Lilly Br. at 53. But Lilly’s post-trial musings on what the jury understood from the instructions is not grounds for a new trial. In any case, if Lilly thought the jury would be aided by a discussion on what it means to enable the “full scope,” it was free to cover that in closing. Dkt. 359, Mem. Op. at 10 n.4. Lilly chose not to do so.

²⁵ The Court also noted that, given both the lack of evidence addressed to the prophylaxis of BPH and the overlapping nature of the two terms, an enablement instruction addressing these terms separately would have been confusing to the jury. Dkt. 359, Mem. Op. at 9.

²⁶ Lilly survived summary judgment by representing to the Court that infringement requires an enlarged prostate. Dkt. 193-1 Lilly Corrected Opp’n to MSJ at 14, *see also* Dkt. 234, Mem. Op. & Order at 18. More recently, Lilly opposed UroPep’s motion for fees on the theory that factual issues concerning the presence of an enlarged prostate needed to be resolved by the jury. Dkt. 374, Lilly Opp’n to Fees Mot. at 2. Lilly’s post-trial argument that infringement does not require an enlarged prostate effectively undercuts its lone argument against paying UroPep’s attorneys’ fees on that issue.

XII. THE REFUSAL TO INSTRUCT THE JURY THAT LAWS OF NATURE ARE NOT PATENTABLE DID NOT PREJUDICE LILLY

Lilly says it was prejudiced by the Court’s decision not to instruct the jury “that the discovery of a law of nature is not, by itself, a patentable invention,” and thus that it deserves a new trial. Lilly Br. at 54. The Court’s previous decision on this issue was correct and Lilly’s request for a new trial should be denied.²⁷

As an initial matter, and as this Court has already acknowledged, any argument related to 35 U.S.C. § 101 is untimely. “Lilly did not plead a section 101 defense in its answer, and nothing in the pretrial proceedings or the presentation of the case to the jury laid a basis for a § 101 defense.” Dkt. 359, Mem. Op. at 13. Lilly says its request for a § 101 instruction was timely because it was not pursuing a § 101 “defense,” but rather seeking a § 101 “instruction” so the jury could “properly evaluate” its invalidity defenses. Lilly Br. at 56. This attempt to introduce a § 101 argument for the first time at trial is unavailing for two reasons.

First, Lilly did not even offer a § 101 instruction in its two proposed jury instructions. *See* Dkt. 250-2, Lilly’s Proposed Jury Instr; Dkt. 317-1, Parties’ Second Proposed Jury Instr Facing a clear waiver of a § 101 instruction, Lilly instead said its proposed § 101 instruction was buried in its inherent anticipation instruction. Ex. A, Tr. at 1366:16-24. But surreptitiously inserting a § 101 instruction into a proposed inherent instruction – after failing to plead a § 101 defense or otherwise preserve the issue – is insufficient to make the request timely.²⁸

²⁷ The parties filed written submissions on whether to provide a § 101 instruction during trial, Dkt. 325, Lilly Notice of Authority; Dkt. 329, UroPep Resp. to Lilly’s Notice of Authority, and the Court found that such an instruction was not warranted. Dkt. 359, Order at 13-14.

²⁸ Lilly says it included its § 101 instruction in the inherent anticipation instruction because a jury would understand it applied generally to invalidity defenses. This retrospective explanation is suspect. If Lilly wanted to offer a general § 101 instruction applicable to all invalidity defenses, it should have proposed it in the general invalidity instruction. Further, the proposed language Lilly cites as evidence it sought a § 101 instruction is a block quote from *EMI Group*

Second, Lilly’s proposed rule – that it did not waive a § 101 instruction even though it did not seek a § 101 defense – creates perverse incentives. Lilly’s proposed rule would allow a party to lie in wait on a § 101 argument until trial by not raising a § 101 defense, but then nonetheless present a § 101 defense to the jury under the guise of providing “context” to its disclosed invalidity defenses. This rule runs counter to the notice policy underlying our system’s disclosure rules, and it is unsurprising that Lilly cites zero case law propounding such a rule.²⁹

Regardless, a § 101 instruction was not warranted because UroPep did not invent a natural phenomenon. It invented a medical treatment. Lilly sought an instruction that UroPep’s invention was “the discovery of a functional role for PDE5 in the male prostate.” Dkt. 325, Lilly Notice at 4. That is not right. UroPep’s invention is a method of treating BPH by using PDE5 inhibitors. UroPep discovered that PDE5 was in the prostate and that PDE5 had a functional role in the prostate by using PDE5 inhibitors in the tissue bath experiment. The invention is the use of PDE5 inhibitors to treat a disease based on the demonstrated effect of PDE5 on prostatic tissue strips. Inventing the use of PDE5 inhibitors to treat a disease by using PDE5 inhibitors in an in vitro assay is permissible; that laws of nature direct how PDE5 inhibitors work is of no import. Dkt. 359, Mem. Op. at 14. (“[A]n *application* of a law of nature to a known structure or process may well be deserving of patent protection.”) *Diamond v. Diehr*, 450 U.S. 175, 187 (1981) (quoting *Parker v. Flook*, 437 U.S. 584, 590 (1978)). (emphasis in original).³⁰

North America, Inc. v. Cypress Semiconductor Corp., 268 F.3d 1342, 1351 (Fed Cir. 2001). But the quoted language is about inherent anticipation, not § 101. *EMI Group*, 268 F.3d at 1351.

²⁹ Further, as the Court previously stated, introducing a § 101 instruction despite no evidence at trial relating to a § 101 defense would be both confusing to the jury and unfairly prejudicial to UroPep. Dkt. 359, Mem. Op. at 13.

³⁰ When Lilly finally offered a § 101 instruction, it stated “there needs to be some instruction that the simple discovery that PDE5 is in the prostate or that PDE5 plays a functional role in the prostate is not, is not part of the analysis for this claim.” Ex. A, Tr. at 1361:16-20. This Court already held that Lilly’s proposed instruction is erroneous because “it is perfectly legitimate for

XIII. THE COURT PROPERLY EXCLUDED THE BUNNAGE APPLICATIONS

In its supplemental invalidity contentions served a month before trial, Lilly identified a new alleged obviousness combination that included a non-prior-art application. *See* Dkt. 253-1, Lilly Second Supp. Invalidity Contentions at 5. That application had been previously identified as “additional prior art” in Lilly’s invalidity contentions, but had never been charted by Lilly or discussed in an expert report. So UroPep filed a motion to strike the application and related documents that Lilly had included on its exhibit list (collectively, the “Bunnage applications”). *See* Dkt. 253, UroPep Mot. to Strike. In opposition, Lilly argued for the first time that the Bunnage applications supported a previously undisclosed “simultaneous invention” theory, and that Lilly should be allowed to use the Bunnage applications to impeach UroPep’s expert, Dr. Bell. *See* Dkt. 256, Lilly Opp’n to UroPep Mot. to Strike at 2-6.

The Court rejected Lilly’s attempt to inject a “simultaneous invention” theory less than a month before trial, finding that this violated “Lilly’s obligations under the Discovery Order” and would “severely prejudice” UroPep. *See* Dkt. 293, Order Granting UroPep Mot. to Strike at 8. However, the Court noted that “Lilly will be permitted to make use of that evidence for impeachment to the extent UroPep opens the door by offering contrary testimony.” *Id.* at 9.

Mindful of the Court’s ruling, UroPep did not offer “contrary testimony” at trial. Lilly tried to open the door by seeking testimony from Dr. Bell that contradicted his deposition testimony. *See* Ex. A, Tr. at 343:14-357:7 (Lilly repeatedly attempting to introduce this evidence). But Lilly was unable to elicit testimony from Dr. Bell contradicting his deposition.

the discovery of the functional role of PDE5 to be part of the analysis of patentability.” Dkt. 359, Mem. Op. at 14 (internal citations and quotation marks omitted). Lilly does not disagree, instead arguing that its statement was a response to statements by UroPep’s counsel. Lilly Br. at 56. This is belied by the transcript, which shows that Lilly offered the above instruction when it first brought up the § 101 issue at the conference. Ex. A, Tr. at 1361:9-20.

See id. at 355:15-22 (the Court noting there was nothing in Dr. Bell’s deposition “that constitutes a representation that he has an independent recollection that’s been refreshed by the” Bunnage applications). Dr. Bell’s testimony, on cross, that he first learned of Pfizer’s efforts to research sildenafil for BPH by reading a much later publication, *id.* at 348:18-349:8, did not contradict his deposition testimony concerning Bunnage. Lilly’s inability to elicit contradictory testimony from Dr. Bell is evidence of Dr. Bell’s honesty; it is not a reason for a new trial.

XIV. UROPEP’S IMPEACHMENT OF DR. ROTELLA WITH HIS OWN PATENT DOES NOT WARRANT A NEW TRIAL

Lilly says it was unfairly prejudiced when UroPep impeached Dr. Rotella with his own patent (the ’368 patent).³¹ Lilly Br. at 59. According to Lilly, the unfair prejudice warrants a new trial; i.e., that a new trial is needed to “prevent an injustice.” *Seibert*, 851 F.3d at 438. But, while devastating, UroPep’s cross-examination of Dr. Rotella was not unfairly prejudicial to Lilly. Rather, it was a reflection of the fact that “the ’368 patent [had] appreciable impeachment value for [noninfringement and invalidity] topics.” Dkt. 264, Mem. Op. at 5. “UroPep [was] entitled to use it to challenge Dr. Rotella’s credibility.” *Id.*

As an initial matter, Lilly contends that UroPep used the ’368 patent to “improperly bolster the validity of the ’124 patent.” Lilly Br. at 59. Not true. At trial UroPep used the ’368 patent only to impeach the conclusions and credibility of Dr. Rotella. The ’368 patent was never admitted as an exhibit at trial, and was not used with any witness other than Dr. Rotella.

³¹ Use of the ’368 patent to impeach Dr. Rotella has been extensively briefed, first as Lilly’s motion *in limine* no. 2 (Dkt. 198, Lilly Mot. in Lim. at 6-8), and then in a joint statement regarding Lilly’s motion *in limine* no. 2. Dkt. 252, Joint Statement at 7-13. The Court has already written an opinion detailing why it denied Lilly’s previous motions. Dkt. 264, Mem. Op. at 2-6. That rejection was within this Court’s discretion. *Hesling v. CSX Transp., Inc.*, 396 F.3d 632, 643 (5th Cir. 2005) (“The grant or denial of a motion *in limine* is considered discretionary, and thus will be reversed only for an abuse of discretion and a showing of prejudice.”).

Instead, UroPep's cross-examination compared Dr. Rotella's trial opinions with what he included in his patent in 1998. Ex. A, Tr. at 798:6-802:1; 821:9-824:3; 829:14-859:10. For example, Dr. Rotella opined that it would have been obvious to a person of skill in July 1997 to treat BPH with a selective PDE5 inhibitor, but when his drug development team listed dozens of therapeutic uses for selective PDE5 inhibitors in the '368 patent (including uses unrelated to ED), BPH was not one of the entries. *Id.* at 821:9-823:15. This is the sort of impeachment testimony the Court contemplated. Dkt. 264, Mem. Op. at 5 (citing Fed. R. Evid. 613).³²

Further, Lilly again tries pointing to differences between the '368 and '124 patent to say UroPep should not have been allowed to impeach Rotella with his own patent. Lilly Br. at 59. For example, Lilly says the '368 patent is limited to compounds with a specified chemical structure, while the '124 patent is not.³³ *Id.* But as this Court noted, if Lilly thought these differences negated any apparent inconsistency between Dr. Rotella's out-of-court and in-court statements, Lilly was free to highlight those differences to the jury. Dkt. 264, Mem. Op. at 4-5.³⁴

XV. CONCLUSION

For the reasons stated above, Lilly's various motions should be denied.

³² Lilly also suggests that certain questions went "well beyond proper cross-examination." Lilly Br. at 59. To the extent Lilly is arguing that a topic was beyond the scope of Lilly's direct exam of Dr. Rotella, Lilly waived that argument when it agreed on the record that it would not raise a scope objection to UroPep's cross examination. Ex. A, Tr. at 265:3-266:9. In exchange, Lilly was allowed to play testimony of UroPep's former expert. *Id.* at 266:10-267:9.

³³ Lilly also asserts, with no citation, that UroPep misled the jury by suggesting that the '368 patent's structurally defined genus of compounds was the same as the '124 patent's functionally defined genus of compounds. Lilly Br. at 59. Even setting aside the lack of citation, UroPep did not mislead the jury; it presented evidence that Dr. Rotella made one statement out of court at the relevant time (the late 1990s), and a different statement in court today.

³⁴ Lilly's contention that it needed more time at trial rings hollow. Lilly Br. at 60. Lilly had ample time to bring four invalidity defenses. It cannot now claim it needed more time for one issue with one witness. Similarly, UroPep's cross of Dr. Rotella was in line with the Court's instruction, Dkt. 264, Mem. Op. at 6, and did not create the mini-trial Lilly had forewarned.

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CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing document was filed electronically in compliance with Local Rule CV-5(a) on July 13, 2017. As such, this document was served on all counsel who are deemed to have consented to electronic service. Local Rule CV-5(a)(3)(A).

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